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L3           345 SEA FILE=CAPLUS ABB=ON  PLU=ON  RUNDFELDT C?/AU OR KIETZMANN
                 M?/AU OR HOPPMANN J?/AU OR BAUMER W?/AU OR BAEUMER W?/AU OR
                 KUSS H?/AU OR HOFGEN N?/AU
L4        384518 SEA FILE=CAPLUS ABB=ON  PLU=ON  SKIN OR ?DERM?
L5            48 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND L4
L6            22 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOPICAL AND L5


=> d ibib ed ab l6 1-22

L6   ANSWER 1 OF 22  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:226501  CAPLUS
DOCUMENT NUMBER:          144:267237
TITLE:                    The phosphodiesterase 4 inhibitor AWD 12-281 is active
                          in a new guinea-pig model of allergic skin
                          inflammation predictive of human skin
                          penetration and suppresses both Th1 and Th2 cytokines
                          in mice
AUTHOR(S):                Hoppmann, Joachim; Baeumer, Wolfgang
                          ; Galetzka, Christin; Hoefgen, Norbert;
                          Kietzmann, Manfred; Rundfeldt, Chris
CORPORATE SOURCE:         Department of Pharmacology, elbion AG, Radebeul,
                          D-01445, Germany
SOURCE:                   .Journal of Pharmacy and Pharmacology (2005), 57(12),
                          1609-1617
                          CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER:                Pharmaceutical Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  14 Mar 2006
AB   The selective phosphodiesterase 4 (PDE4) inhibitor AWD 12-281 is
     structurally optimized for topical administration.  It has
     potent effects in models of lung inflammation if administered as a dry
     powder inhalation.  It has also demonstrated its anti-inflammatory
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property in a mouse model of cutaneous inflammation after **topical** administration. The aim of this study was to evaluate whether AWD 12-281 may be capable of penetrating human **skin**. Therefore a new guinea-pig model of allergic **skin** inflammation had to be developed. In ovalbumin-sensitized guinea-pigs, intracutaneous administration of ovalbumin results in a rapid development of allergic **skin** wheals. Topically administered AWD 12-281 was capable of reducing the development of wheals, indicating that this compound can penetrate the stratum corneum of guinea-pig **skin** as a predictor of human **skin** penetration. A secondary aim was the evaluation of a T cell subtype preference of AWD 12-281 since PDE4 inhibitors are said to preferentially inhibit Th2-type cytokines. Therefore, the effects of AWD 12-281 on a broad spectrum of Th1- and Th2-type cytokines were studied in tissue homogenates after allergen challenge in sensitized mice and in supernatants of anti CD3/anti-CD28-stimulated peripheral blood mononuclear cells (PBMCs). In both models, AWD 12-281 suppressed both T cell subtype cytokines indicating a broad spectrum activity of AWD 12-281. A further issue was to determine the duration of action and the concentration-response relation of the **topical** activity of AWD 12-281 using a model of acute local inflammation - the arachidonic-acid-induced mouse ear edema. The compound exhibited a dose-dependent effect with a minimally effective concentration of 0.3%; after repeated administration the minimally effective concentration was 0.03%. A single administration of a 3% solution resulted in significant suppression of inflammation even 48 h after treatment. In conclusion, our results indicate that AWD 12-281 is a very promising drug candidate not only for the treatment of lung inflammation using inhalative administration but also for the treatment of atopic **dermatitis**.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:42181 CAPLUS
DOCUMENT NUMBER: 144:305549
TITLE: Influence of purinergic substances on proliferation of murine keratinocytes and full-thickness **skin** healing
AUTHOR(S): Braun, M.; Lelieur, K.; **Kietzmann, M.**
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, Hannover Foundation, University of Veterinary Medicine, Hannover, Germany
SOURCE: Advances in Veterinary Dermatology (2005), 5, 203-209
CODEN: AVDEEA; ISSN: 1366-185X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 17 Jan 2006
AB Purinoceptors are membrane-bound receptors for adenosine, purines and pyrimidines that are expressed in nearly all cell types throughout the organism. Previous studies have demonstrated that they are involved in the regulation of proliferation and differentiation of most target cells. As it is well-known that several purinoceptors are expressed in **skin** keratinocytes, we were interested in examining their involvement in wound healing. The expression of the receptors A2B, P2Y1, P2Y2 and P2Y6 was previously demonstrated in the murine keratinocyte cell line MSC-P5. Therefore, we performed proliferation assays with various purinoceptor agonists and antagonists in these cells. The proliferation was determined by incorporation of 5-bromo-2-deoxyuridine (BrdU). The purinoceptor agonists ATP (ATP), uridine triphosphate (UTP) and 5'-(N-ethyl)-carboxamidoadenosine (NECA) enhanced the cell growth of

MSC-P5 cells in vitro. The mitogenic effect of ATP and UTP was inhibited by the non-selective P2Y-receptor antagonist suramin, while the effect of NECA was inhibited by the selective A2B-receptor antagonist enprofylline. For in vivo studies, female NMRI mice were used. To impair the wound healing process, animals were treated once daily with dexamethasone. After a week of treatment, full-thickness wounds were set with biopsy punches in depilated back **skin** and the purinoceptor agonists and antagonists were administered once daily topically on the wound area. The wound healing process was measured by determination of the wound area. **Topical** treatments with both NECA and UTP induced better wound healing in dexamethasone-treated mice, which was comparable to the control group without dexamethasone treatment. These studies confirm that pharmacol. actions via purinoceptors offer an intriguing possibility in the treatment of impaired wound healing. Nevertheless, further investigations are needed to fully elucidate the role of purinergic mechanisms involved in wound healing.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:42174 CAPLUS
DOCUMENT NUMBER: 144:324423
TITLE: Effects of the immunomodulatory drugs tacrolimus, rapamycin and cilomilast on dendritic cell function in a rodent model of allergic contact **dermatitis**
AUTHOR(S): **Baeumer, W.**; Suelzle, B.; Weight, H.; Hecht, M.; **Kietzmann, M.**
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, University of Veterinary Medicine Hannover Foundation, Hannover, Germany
SOURCE: Advances in Veterinary Dermatology (2005), 5, 89-96
CODEN: AVDEEA; ISSN: 1366-185X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 17 Jan 2006
AB The in vitro and in vivo immunomodulatory effects of the phosphodiesterase-4 inhibitor cilomilast were compared to tacrolimus and rapamycin, immunosuppressive drugs for use in organ transplantation. Tacrolimus is also registered for treatment of human atopic **dermatitis.** In vitro, the effect of these agents on the mixed leukocyte reaction (dendritic cell-mediated T-cell activation) was tested. Cilomilast and tacrolimus, as well as rapamycin, were able to inhibit proliferation in a dose-dependent manner. In vivo, the inhibitory action of the immunomodulatory drugs was compared in the toluene-2,4-diisocyanate (TDI)-induced allergic inflammatory response. After **topical** administration, cilomilast and tacrolimus, but not rapamycin, inhibited the inflammatory response. Only combined **topical** and systemic administration of rapamycin caused a distinct inhibition of the allergic reaction. Cilomilast (20 mg/kg) and rapamycin (20 mg/kg) as well as tacrolimus (2.5 mg/kg) were administered i.p. at 16 and 0.5 h before challenge, and topically onto mouse ears (cilomilast 3%, rapamycin 1%, tacrolimus 0.5%) 2 h before challenge. All substances induced a significant inhibition of the ear swelling measured 16 h after TDI challenge, accompanied by a reduction of the draining auricular lymph node weight and lymphocyte cell count. Corresponding to this, the d. of Langerhans cells in the **epidermis** was higher in cilomilast-, tacrolimus- and rapamycin-treated mice compared with vehicle-treated mice. Dendritic cell migration, as measured in a **skin** dendritic cell migration

assay on cultivated ears, was also significantly inhibited by all agents.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:966451 CAPLUS
DOCUMENT NUMBER: 143:318705
TITLE: Cilomilast, tacrolimus and rapamycin modulate dendritic cell function in the elicitation phase of allergic contact **dermatitis**
AUTHOR(S): **Baeumer, W.**; Suelzle, B.; Weigt, H.; De Vries, V. C.; Hecht, M.; Tschernig, T.; **Kietzmann, M.**
CORPORATE SOURCE: Departments of Pharmacology, Toxicology and Pharmacy, University of Veterinary Medicine Hannover, Foundation, Hannover, 30559, Germany
SOURCE: British Journal of Dermatology (2005), 153(1), 136-144
CODEN: BJDEAZ; ISSN: 0007-0963
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Sep 2005
AB Cilomilast and tacrolimus as well as rapamycin are potential drugs for the treatment of allergic **skin** diseases like atopic **dermatitis** and allergic contact **dermatitis.** To compare the in vitro and in vivo immunomodulatory effects of the phosphodiesterase 4 inhibitor cilomilast with those of tacrolimus and rapamycin. The in vitro action of cilomilast, tacrolimus and rapamycin were tested in a mixed leukocyte reaction (MLR). In vivo, the inhibitory action of the immunomodulatory drugs was compared in the toluene-2,4-diisocyanate (TDI)-induced allergic inflammatory response with particular focus on dendritic cell (DC) function. Cilomilast, tacrolimus and rapamycin were all able to inhibit DC-mediated T-cell activation in a MLR. But it was demonstrated for cilomilast that the target cells are T cells rather than DC. In vivo, a combination of systemic and **topical** administration of each of these three substances significantly inhibited swelling in the murine ear 16 h after TDI challenge. There was also a reduction in the weight of the draining auricular lymph node, in lymphocyte cell count, and in the number of emigrated DC. The d. of Langerhans cells in the **epidermis** was correspondingly higher in mice treated with cilomilast, tacrolimus and rapamycin than in those treated with vehicle. All three substances were found to inhibit DC migration ex vivo in a **skin** DC migration assay performed on ear tissue after TDI challenge. DC migration into the draining lymph node also takes place in the elicitation phase of allergic contact **dermatitis** and this migration can be influenced by tacrolimus and rapamycin, and, to a lesser extent, by cilomilast.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:60309 CAPLUS
DOCUMENT NUMBER: 140:105273
TITLE: **Topical** treatment of **skin** diseases
INVENTOR(S): **Rundfeldt, Chris**; **Kietzmann, Manfred**; **Hoppmann, Joachim**; **Baeumer, Wolfgang**; **Kuss, Hildegard**; Hoefgen, Norbert
PATENT ASSIGNEE(S): Elbion AG, Germany

SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004006920	A1	20040122	WO 2003-EP7514		20030710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO; RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004038958	A1	20040226	US 2003-611649		20030701
CA 2492093	AA	20040122	CA 2003-2492093		20030710
AU 2003254332	A1	20040202	AU 2003-254332		20030710
BR 2003012696	A	20050426	BR 2003-12696		20030710
EP 1531818	A1	20050525	EP 2003-763810		20030710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1681500	A	20051012	CN 2003-821520		20030710
JP 2005537262	T2	20051208	JP 2004-520586		20030710
ZA 2005000108	A	20050223	ZA 2005-108		20050106
NO 2005000718	A	20050401	NO 2005-718		20050210
PRIORITY APPLN. INFO.:			US 2002-395221P	P	20020711
			WO 2003-EP7514	W	20030710

OTHER SOURCE(S): MARPAT 140:105273
ED Entered STN: 26 Jan 2004
AB The present invention relates to a method for the treatment of an inflammatory and/or allergic **skin** disease comprising topically administering a substituted hydroxy indole which is a phosphodiesterase 4 inhibitor. Examples are provided of the **topical** effectiveness of AWD 12-281 and cilomilast in **dermal** immunol. inflammation.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:924091 CAPLUS
DOCUMENT NUMBER: 140:157041
TITLE: Effects of cilomilast on dendritic cell function in contact sensitivity and dendritic cell migration through **skin**
AUTHOR(S): **Baumer, Wolfgang**; Tschernig, Thomas; Sulzle, Boris; Seegers, Ulrike; Luhrmann, Anke; **Kietzmann, Manfred**
CORPORATE SOURCE: Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hannover, D-30559, Germany
SOURCE: European Journal of Pharmacology (2003), 481(2-3), 271-279
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal

LANGUAGE: English
ED Entered STN: 26 Nov 2003
AB The phosphodiesterase 4 inhibitor cilomilast demonstrated strong inhibitory effects in a model of allergic contact **dermatitis.** In this study, we examined whether this inhibitory effect is at least partly due to modulation of dendritic cell function. Bone marrow-derived dendritic cells were pulsed with the sensitizer toluene-2,4-diisocyanate and administered s.c. to nonsensitized mice. Five days later, the mice were challenged with a low dose of toluene-2,4-diisocyanate onto the ears. In contrast to sham-treated mice, mice obtaining toluene-2,4-diisocyanate pulsed dendritic cells showed a significant increase in ear swelling. This swelling was not influenced when the dendritic cells were pre-incubated with cilomilast. When cilomilast was administered systemically simultaneously to the application of toluene-2,4-diisocyanate pulsed cells, there was an impaired allergic reaction provoked 5 days later. Addnl., a **topical** treatment with cilomilast resulted in a significant inhibition of **skin** dendritic cell migration. These results indicate that the antigen-presenting function of dendritic cells is not influenced by cilomilast but the dendritic cell T cell interaction and dendritic cell migration is modulated.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:695438 CAPLUS
DOCUMENT NUMBER: 140:87294
TITLE: AWD 12-281, a highly selective phosphodiesterase 4 inhibitor, is effective in the prevention and treatment of inflammatory reactions in a model of allergic **dermatitis**
AUTHOR(S): **Baeumer, Wolfgang**; Gorr, Gilbert; **Hoppmann, Joachim**; Ehinger, Andreas M.; **Rundfeldt, Chris**; **Kietzmann, Manfred**
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, School of Veterinary Medicine, Hannover, D-30559, Germany
SOURCE: Journal of Pharmacy and Pharmacology (2003), 55(8), 1107-1114
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Sep 2003
AB AWD 12-281 (N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide), a phosphodiesterase 4 inhibitor, which is optimized for **topical** administration, was tested in a model of allergic **dermatitis** in mice. To obtain an allergic **dermatitis**, BALB/c mice were sensitized to toluene-2,4-diisocyanate (TDI). The allergic reaction was challenged by **topical** administration of TDI onto the mice ears. AWD 12-281 was tested for its anti-inflammatory potential by oral, i.p. and **topical** administration. The phosphodiesterase 4 inhibitor, cilomilast (SB 207499), and/or the corticosteroid, diflorasone diacetate, were used as reference compds. Given orally and i.p. 2 h before as well as 5 and 24 h after TDI challenge, AWD 12-281 showed no, or only a transient inhibition of the allergen-induced ear swelling, whereas cilomilast significantly inhibited this ear swelling. Applied topically onto the ears before TDI challenge, AWD 12-281, cilomilast and diflorasone diacetate caused total inhibition of ear swelling 24 h after challenge, confirmed by a decrease of the pro-inflammatory cytokines interleukin-4,

interleukin-6 and macrophage inhibitory protein-2. Administered topically after TDI challenge as therapeutic intervention, AWD 12-281 and diflorasone diacetate caused significant inhibition of ear swelling; cilomilast failed to do so. These results indicate that topically administered AWD 12-281 may be potent in the prevention and treatment of allergic/inflammatory **skin** diseases.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:495906 CAPLUS
DOCUMENT NUMBER: 138:117605
TITLE: Effects of the phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on the inflammatory reaction in a model of allergic **dermatitis**
AUTHOR(S): **Baumer, Wolfgang**; Gorr, Gilbert; **Hoppmann, Joachim**; Ehinger, Andreas M.; Ehinger, Britt; **Kietzmann, Manfred**
CORPORATE SOURCE: Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hanover, 30559, Germany
SOURCE: European Journal of Pharmacology (2002), 446(1-3), 195-200
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Jul 2002
AB The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast, c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were tested in a model of allergic **dermatitis** in mice. To obtain an allergic **dermatitis**, BALB/c mice were sensitized to toluene-2,4-diisocyanate. The allergic reaction was challenged by **topical** administration of toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups of mice were treated topically (ear **skin**) with SB 207499 or AWD 12-281. There was a significant ear swelling in toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after challenge. SB 207499 and AWD 12-281 inhibited this swelling significantly 8, 16, 24 and 48 h after the challenge. For biochem. parameters and histol., ears were sampled from mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue, SB 207499 and AWD 12-281 inhibited significantly the secretion of interleukin 1β induced by toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx (granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and 16 h after challenge was nearly abolished by AWD 12-281 and SB 204799.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:401655 CAPLUS
DOCUMENT NUMBER: 135:174923
TITLE: Effects of steroidal and non-steroidal antiphlogistic drugs on eicosanoid synthesis in irritated **skin**: studies with the isolated perfused bovine udder
AUTHOR(S): **Baumer, Wolfgang**; **Kietzmann, Manfred**
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, School of Veterinary Medicine, Hannover, 30559, Germany

SOURCE: Journal of Pharmacy and Pharmacology (2001), 53(5), 743-747
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Jun 2001
AB Using the isolated perfused bovine udder as an in-vitro model of **skin** inflammation, the effects of topically administered arachidonic acid on prostaglandin and leukotriene synthesis have been shown previously. In this study, the effects of indometacin (indomethacin) and clobetasol-17-propionate (administered topically) as well as flunixin meglumine and meloxicam (administered via the perfusion fluid) have been studied. Compared with controls, arachidonic acid caused a significant increase in the **dermal** prostaglandin E2 (PGE2) and peptidoleukotriene (LTC4/D4/E4) concentration **Topical** treatment with indometacin (1.6 mg cm-2) and clobetasol-17-propionate (90 μg cm-2), which were administered 60 min before arachidonic acid administration, inhibited the inflammatory reaction. Flunixin meglumine (1 μg mL-1 perfusion fluid) was administered 30 min after and meloxicam (3 μg mL-1 perfusion fluid) was administered 60 min before arachidonic acid application. Three hours after arachidonic acid administration, a significant inhibition of PGE2 synthesis was induced by flunixin. In contrast, meloxicam showed only a slight effect. The effect of flunixin was comparable with in-vivo results. It is known from animal studies that anti-inflammatory effects of meloxicam are obvious within up to 6 h after treatment. Therefore, the incomplete effect of meloxicam may be explained pharmacokinetically. In conclusion, the described in-vitro model seems to be suitable for studies of pharmacol. effects on eicosanoid synthesis in the **skin.**
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:550078 CAPLUS
DOCUMENT NUMBER: 134:25090
TITLE: Application of deuterated benzoyl peroxide in an in vitro model of percutaneous absorption and **dermal** metabolism of chemical substances
AUTHOR(S): Blume, B.; **Kietzmann, M.**; Moder, M.; Kranke, P.; Wahren, M.
CORPORATE SOURCE: Faculty of Veterinary Medicine, Institute of Pharmacology, Pharmacy and Toxicology, University of Leipzig, Leipzig, D-04103, Germany
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds 1997, Proceedings of the International Symposium, 6th, Philadelphia, PA, United States, Sept. 14-18, 1997 (1998), Meeting Date 1997, 597-600. Editor(s): Heys, J. Richard; Melillo, David G. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69AGFQ
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 11 Aug 2000
AB The percutaneous absorption and metabolism of deuterated benzoyl peroxide was investigated following **topical** administration on isolated perfused bovine udder. Benzoyl peroxide-d10 was detected in the perfusate 30-60 min after application. Its metabolite benzoic acid-d5 was detected in the perfusate at much lower concentration for a longer time.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:280377 CAPLUS
TITLE: Deuterium labelling in investigations of **transdermal** resorption and **intradermal** metabolism of chemical compounds
AUTHOR(S): **Kietzmann, M.**; Blume, B.; Moder, M.; Kranke, P.; Wahren, M.
CORPORATE SOURCE: Faculty of Veterinary Medicine, Institute of Pharmacology, Pharmacy and Toxicology, University of Leipzig, Leipzig, Germany
SOURCE: Isotopes in Environmental and Health Studies (1998), 34(1-2), 157
CODEN: IEHSF8; ISSN: 1025-6016
PUBLISHER: Gordon & Breach Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 May 2000
AB Isolated perfused udders from slaughtered cows have been introduced as a new in vitro model for **transdermal** penetration and absorption studies [1]. It allows to determine the consequences of **skin** contact of chemical substances without sacrificing laboratory animals. Benzoyl peroxide 1 is a component of some drug formulations for **topical** application. Administration of 500mg 1 on an udder **skin** area of 100cm2 resulted in absorption and metabolism While unchanged I could be detected in the **skin** tissue, only the metabolite benzoic acid 2 was found in the perfusate (heparinized tyrode solution) in expts. without labeling [1]. The use of 1-d10 instead of 1 under identical conditions resulted in a significant lower detection limit (GC-MS, selected ion monitoring mode, internal stds. unlabeled 1 and 2). In perfusate samples taken between 30 and 105 min after application small amts. of 1-d10 were detected with a rather sharp maximum of 10 ng/g in the 45 min sample. The concentration of the metabolite 2-d5 in the perfusate rose gradually from 15 min. to a flat maximum at about 105 min. and was tell detectable 150 min. after application of 1-d10. Other metabolites were not detected, a special search was made for deuterated hydroxybenzoic acids. We wish to point out, that this reversal of a standard anal. method (quantification of mass-spectrometric trace detns. by use of labeled compds. as internal stds.) should be of advantage in similar problems, if the chemical substance or their metabolites are either ubiquitous or physiol.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:221539 CAPLUS
DOCUMENT NUMBER: 133:450
TITLE: Effects of the phosphodiesterase 4 inhibitor RPR 73401 in a model of immunological inflammation
AUTHOR(S): Ehinger, A. M.; Gorr, G.; **Hoppmann, J.**; Telser, E.; Ehinger, B.; **Kietzmann, M.**
CORPORATE SOURCE: Institute of Pharmacology, Toxicol. and Pharm., School of Veterinary Medicine, Hannover, 30559, Germany
SOURCE: European Journal of Pharmacology (2000), 392(1/2), 93-99
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal

LANGUAGE: English
ED Entered STN: 06 Apr 2000
AB The study was performed to investigate effects of the phosphodiesterase 4 inhibitor RPR 73401 [N-(3,5-dichloropyrid-4-yl)-3-cyclopentyl-oxy-4-methoxybenzamid] on an allergic **skin** reaction. To simulate an immunol. inflammation, BALB/c mice were sensitized to dinitrochlorobenzene or toluene diisocyanate. At first, the abdominal **skin** was shaved and 50 μl Freund's adjuvant were injected intracutaneously once. Then, the horny layer was removed by adhesive tape stripping and 100 μl 0.5% dinitrochlorobenzene or 5% toluene diisocyanate were administered on the **epidermis** for 4 days. After repeated local treatment of the ear **skin** with 20 μl 3% RPR 73401 or i.p. administration of 1 and 5 mg/kg RPR 73401, 20 μl 1% dinitrochlorobenzene or 0.5% toluene diisocyanate were given topically as a challenge. The vehicle controls showed a high increase in ear thickness over 48 h after challenge, whereas RPR 73401 administered on either route reduced this increase significantly. Nevertheless after **topical** administration, RPR 73401 had a longer lasting effect. These and other results may point to an indication for RPR 73401 in immunol. **dermatitis.**
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:6444 CAPLUS
DOCUMENT NUMBER: 132:74708
TITLE: Application of deuterated compounds for investigations of percutaneous absorption of chemical substances
AUTHOR(S): **Kietzmann, M.**; Kranke, P.; Moder, M.; Schrader, S.; Wahren, Manfred
CORPORATE SOURCE: Institute Pharmacology Toxicology Pharmacy, School Veterinary Medicine, Hannover, Germany
SOURCE: Isotopes in Environmental and Health Studies (1999), 35(1-2), 127-134
CODEN: IEHSF8; ISSN: 1025-6016
PUBLISHER: Gordon & Breach Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Jan 2000
AB The percutaneous absorption of the xenoestrogen 2,2-bis-(4-hydroxyphenyl)-propane (bisphenol A) was studied and compared with results on dibenzoyl peroxide, a component of drug formulations for **topical** application. Isolated perfused bovine udders from slaughtered cows were employed as models for human **skin.** The deuterium labeled compds. bisphenol A-d14 and dibenzoyl peroxide-d10 were applied to enhance the reliability of GC-MS trace detns. by use of reverse isotope dilution anal. Bisphenol A-d14 was found in perfusate and milk equivalent samples obtained between 60 and 300 min after **topical** application with maximum concns. between 120 and 180 min. Bisphenol A-d14 was enriched in the milk samples by a factor of about 300 compared with the perfusate. The results confirm a possible penetration of bisphenol A from the environment through the **skin** into the capillary system. Dibenzoyl peroxide studied on the same model system penetrated faster than bisphenol A by a factor of about 3.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:603393 CAPLUS
DOCUMENT NUMBER: 129:213553
TITLE: The isolated perfused bovine udder. A model for

detection of UV-induced **skin** damage
AUTHOR(S): Koehler, Petra; Borchert, Stefan; Petersen, Rolf-Dieter; **Kietzmann, Manfred**; Blume, Bettina; **Baeumer, Wolfgang**; Itzel-Kietzmann, Verena-Maria
CORPORATE SOURCE: Chemisches Lab. Dr. Kurt Richter G.m.b.H., Berlin, D-12159, Germany
SOURCE: SOFW Journal (1998), 124(10), 624,626,628-629
CODEN: SOFJEE; ISSN: 0942-7694
PUBLISHER: Verlag fuer Chemische Industrie H. Ziolkowsky
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 23 Sep 1998
AB The biol. activity was demonstrated of a cosmetic active in a finished formulation using the isolated perfused bovine udder. To ensure rapid penetration of the test substances through the stratum corneum, the lipid barrier of the udder **skin** was damaged by repeated **topical** application of aceton, test samples were applied, and the **skin** was UV-irradiated. The DNA newly synthesized during repair was detected by determination of the incorporation rate of bromodeoxyuridine (BrdU), directly indicating the amount of DNA repair. The effect on DNA repair after UV irradiation produced by test sample RP-1 (containing lysate of Bifido bacteria as active principle, available as Repair Complex CLR) was assessed on udders. The rates of BrdU incorporation were determined as optical d. (OD 410 nm) values as a function of exposure time. The test sample led to an increased rate of BrdU incorporation after UV irradiation of the **skin.** Maximum DNA repair was reached after an irradiation time of 3 min. The intact living **skin** of the udder allowed to observe effects in the field of **skin** protection that otherwise were only pursued in vivo (using invasive methods). A review with 13 refs., describing isolated perfused bovine udder as a model for investigation of **transdermal** resorption of substances, UV-induced **skin** damage, and proof of DNA repair activity, was added.

L6 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:311875 CAPLUS
DOCUMENT NUMBER: 127:39606
TITLE: Percutaneous absorption of betamethasone from different formulations using the isolated perfused bovine udder
AUTHOR(S): **Kietzmann, M.**; Blume, B.
CORPORATE SOURCE: Fac. Veterinary Med., Inst. Pharmacology, Pharmacy and Toxicology, Univ. Leipzig, Germany
SOURCE: In Vitro Toxicology (1997), 10(1), 11-15
CODEN: IVTOE4; ISSN: 0888-319X
PUBLISHER: Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 16 May 1997
AB Using udders from slaughtered cows, the percutaneous absorption of betamethasone-17,21-dipropionate was tested. The organ was perfused with gassed Tyrode solution for up to 6 h. A region of udder **skin** (100 cm2) was treated topically with betamethasone-17,21-dipropionate as an ingredient of solution, cream, and ointment (Diprosone) and as ingredient of gel and ointment (Diprosis, with propylene glycol as an addnl. ingredient). Betamethasone-17,21-dipropionate (Diprosone) was also administered on **skin** areas treated with acetone to disorganize the horny layer. The concentration of betamethasone-17,21-dipropionate was measured in perfusate fractions by HPLC. A maximum absorption rate of betamethasone-17,21-dipropionate was found after administration of the

ointment with propylne glycol (Diprosis ointment). The treatment with acetone caused an increase of the absorption rate after application of betamethasone-17,21-dipropionate as ointment, while no increase was measurable after administration of the solution The isolated perfused bovine udder is an in vitro model, which maintains bovine udder **skin** with an isolated vasculature in a viable state. Using this in vitro model, it is possible to compare the **dermal** penetration and absorption of substances after **topical** administration of different drug formulations.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:381767 CAPLUS
DOCUMENT NUMBER: 122:142309
TITLE: Absorption of isosorbide dinitrate after administration as spray, ointment and microemulsion patch. An in-vitro study using the isolated perfused bovine udder
AUTHOR(S): **Kietzmann, M.**; Wenzel, B.; Loescher, W.; Lubach, D.; Mueller, B. W.; Blume, H.
CORPORATE SOURCE: Department Pharmacology, Toxicology and Pharmacy, School Veterinary Medicine, Hannover, Germany
SOURCE: Journal of Pharmacy and Pharmacology (1995), 47(1), 22-5
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Royal Pharmaceutical Society of Great Britain
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Mar 1995
AB The isolated perfused bovine udder is an in-vitro model, which maintains bovine udder **skin** with an isolated vasculature in a viable stage. Using this in-vitro model, the percutaneous absorption and metabolism of isosorbide dinitrate (ISDN) was studied. The organ was perfused with gassed Tyrode solution for up to 6 h. A region of udder **skin** was treated topically with 60 mg ISDN as a spray, 60 mg ISDN as an ointment and with 120 mg ISDN as a microemulsion patch of 30 cm2. Spray and ointment were applied onto a **skin** region of 400 cm2. The concns. of ISDN and its metabolites isosorbide-2-mononitrate and isosorbide-5-mononitrate were measured in perfusate fractions by capillary column gas chromatog. with electron capture detection. Following **topical** administration of the different formulation, ISDN as well as its metabolites were detected in the perfusate fractions, thus demonstrating that ISDN is metabolized by the udder **skin** in-vitro. A maximum amount of ISDN was absorbed after administration as a spray followed by ointment and microemulsion (5, 2.5 and 1.8 μmol total organic nitrate, resp.). In contrast, the ISDN flux per cm2 **skin** was significantly higher after administration of the microemulsion (64.4 pmol cm-2 min-1 for the microemulsion compared with 21.9 and 10.2 pmol cm-2 min-1 for spray and ointment).

L6 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:207830 CAPLUS
DOCUMENT NUMBER: 120:207830
TITLE: The isolated perfused bovine udder as an in vitro model of percutaneous drug absorption. **Skin** viability and percutaneous absorption of dexamethasone, benzoyl peroxide, and etofenamate
AUTHOR(S): **Kietzmann, Manfred**; Loescher, Wolfgang; Arens, Dorothee; Maass, Petra; Lubach, Dietrich

CORPORATE SOURCE: Dep. Pharmacol., Toxicol. Pharm., Sch. Vet. Med., Hannover, D-3000/71, Germany
SOURCE: Journal of Pharmacological and Toxicological Methods (1993), 30(2), 75-84
CODEN: JPTMEZ; ISSN: 1056-8719
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Apr 1994
AB Using udders from slaughtered cows as a new in vitro model of percutaneous drug absorption, the tissue viability and the percutaneous absorption of dexamethasone, benzoyl peroxide, and etofenamate were studied. The organ was perfused with gassed tyrode solution for ≤6 h. As shown by measurement of glucose consumption, lactate production, lactate dehydrogenase activity, and pH in the perfusate, the tissue was viable over a 6-h period. This was confirmed by a histol. examination Determination of the udder **skin**-fold thickness demonstrated that no edema developed within the perfusion period. A maximum **skin** penetration of dexamethasone was found after administration of dexamethasone dissolved in acetone with DMSO, followed by ointment with salicylic acid, ointment without salicylic acid, and acetone solution Expts. with benzoyl peroxide and etofenamate demonstrated that the perfused udder **skin** was capable of metabolizing drugs in vitro. In conclusion, the isolated perfused bovine udder is a new in vitro model, which maintains bovine udder **skin** with an isolated vasculature in a viable state. Using this in vitro model, the authors note it is possible to compare the **dermal** penetration, metabolism, and absorption of substances after **topical** administration of different drug formulations.

L6 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:573471 CAPLUS
DOCUMENT NUMBER: 119:173471
TITLE: The use of material from slaughtered animals for drug testing. Suitability of the bovine udder for studies of **dermal** absorption
AUTHOR(S): **Kietzmann, M.**; Loescher, W.
CORPORATE SOURCE: Inst. Pharmakol. Toxikol. Pharm., Tieraerztl. Hochsch. Hannover, Hannover, W-3000/71, Germany
SOURCE: DTW, Deutsche Tieraerztliche Wochenschrift (1993), 100(2), 54-7
CODEN: DDTWDG; ISSN: 0341-6593
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 30 Oct 1993
AB The suitability of the isolated perfused cows' udder for the testing of **transdermal** drug formulations is illustrated with reference to the authors' previously published work. Data are thus given from studies with dexamethasone, benzoyl peroxide, and isosorbide dinitrate showing the time-dependence of percutaneous absorption and demonstrating that the monitoring of the metabolism of an applied drug is indeed possible with this system.

L6 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:52630 CAPLUS
DOCUMENT NUMBER: 118:52630
TITLE: Studies on the percutaneous absorption of dexamethasone using a new in vitro model, the isolated perfused bovine udder
AUTHOR(S): **Kietzmann, M.**; Arens, D.; Loescher, W.; Lubach, D.

CORPORATE SOURCE: Dep. Pharmacol., Toxicol. Pharm., Sch. Vet. Med., Hannover, D-3000/71, Germany
SOURCE: Predict. Percutaneous Penetration (1991), 519-26. Editor(s): Scott, R. C. IBC Tech. Serv.: London, UK. CODEN: 58EGAN
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 16 Feb 1993
AB Using the isolated perfused bovine udder as an in vitro model, the percutaneous absorption of dexamethasone was studied. A region of udder **skin** (100 cm2) was treated topically with 8 mg dexamethasone (ointment, ointment with addition of 0.5% salicylic acid, solution in acetone, solution in acetone with addition of 10% DMSO). Thereafter, the perfusate was collected and the concentration of dexamethasone in perfusate fractions and in the **skin** biopsies was measured by RIA. The amount of absorbed dexamethasone was also calculated and correlated to the perfusion flux. A maximum **skin** penetration of dexamethasone was found after administration of dexamethasone solubilized in acetone/DMSO, followed by salicylic acid ointment, ointment without salicylic acid, and acetone solution Using the isolated perfused bovine udder, the comparison of **dermal** penetration rates after **topical** administration of drug formulations is possible.

L6 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:400130 CAPLUS
DOCUMENT NUMBER: 117:130
TITLE: Incorporation of tritiated thymidine, leucine, and histidine in murine tail **epidermis** after **skin** irritation (histoautoradiography)
AUTHOR(S): **Kietzmann, M.**; Lubach, D.; Muether, T.
CORPORATE SOURCE: Inst. Pharmakol. Toxikol. Pharm., Tieraerztl. Hochsch., Hannover, W-3000, Germany
SOURCE: DTW, Deutsche Tieraerztliche Wochenschrift (1991), 98(12), 453-6 CODEN: DDTWDG; ISSN: 0341-6593
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 11 Jul 1992
AB Histoautoradiog. detns. of thymidine (I) incorporation into **epidermal** DNA and leucine (II) and histidine (III) incorporation into proteins were employed to study changes in **epidermal** metabolism in mice in the murine tail assay model of **skin** irritation commonly employed to study effects in pathophysiol. **epidermal** processes. Thus, irritation either mech. (abrasion with sandpaper) or chemical (with C16H34) or after hyperproliferation induction by maintenance on essential fatty acid-deficient diets resulted in an increased I labeling index and a **skin** thickening. II was incorporated predominantly in basal **epidermal** cell layers, yet III predominantly in the granular layer. Mech. irritation induced the greatest differences in amino acid localization.

L6 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:135744 CAPLUS
DOCUMENT NUMBER: 114:135744
TITLE: Inhibition of n-hexadecane-induced **epidermal** hyperplasia due to systemically administered ciclosporin
AUTHOR(S): Lubach, D.; **Kietzmann, M.**
CORPORATE SOURCE: Dep. Dermatol., Sch. Med., Hannover, Germany
SOURCE: Arzneimittel-Forschung (1991), 41(2), 137-40

CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Apr 1991
AB **Epidermal** hyperplasia was induced in hairless mice (h/h) by **topical** n-hexadecane treatment of tail and back **skin.** Following this **skin** irritation, a granular layer developed in interfollicular regions of the tail **epidermis.** An increase of ornithine decarboxylase activity, of thymidine triphosphate incorporation into DNA and of amino acid incorporation into protein was found. Shown histol. and by measurement of the called biochem. parameters, ciclosporin (cyclosporin A) (CAS 59865-13-3) (pretreatment with 30 mg/kg/day s.c. for 7 days) inhibited the development of **epidermal** hyperplasia in back and tail **epidermis.**

L6 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:51293 CAPLUS
DOCUMENT NUMBER: 110:51293
TITLE: Effect of benzoyl peroxide in the **epidermis** of mice
AUTHOR(S): **Kietzmann, M.**; Lubach, D.
CORPORATE SOURCE: Inst. Pharmakol. Toxikol. Pharm., Tieraerztl. Hochsch. Hannover, Hannover, D-3000/71, Fed. Rep. Ger.
SOURCE: DTW, Deutsche Tieraerztliche Wochenschrift (1988), 95(5), 197-200
CODEN: DDTWDG; ISSN: 0341-6593
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 17 Feb 1989
AB The **topical** application of benzoyl peroxide (I) to the ears and tails of mice resulted in decreased DNA polymerase activity, protein synthesis, and leucine incorporation of the **epidermis**, without affecting histidine incorporation. **Epidermis** thickness increased, whereas the relation of thickness to cell count decreased. Effects in the tail **epidermis** were not so pronounced as those in the ear. Thus, I induces changes in **epidermal** metabolism, leading to retention acanthosis.

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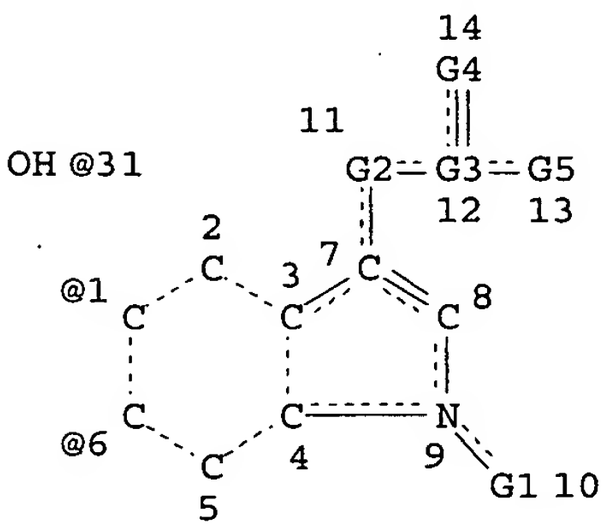

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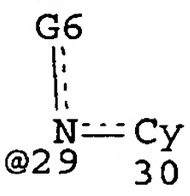

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FILE LAST UPDATED: 21 Sep 2006  (20060921/ED)

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L8       1040261 SEA FILE=REGISTRY ABB=ON  PLU=ON  NC4-C6/ES
L10              STR
L12          250 SEA FILE=REGISTRY SUB=L8 SSS FUL L10
L13          122 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12
L18        21240 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SKIN DISEASES+PFT,NT,OLD/CT
L19       111286 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SKIN/CW
L20         2341 SEA FILE=HCAPLUS ABB=ON  PLU=ON  INTEGUMENT?
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L24           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 OR L21


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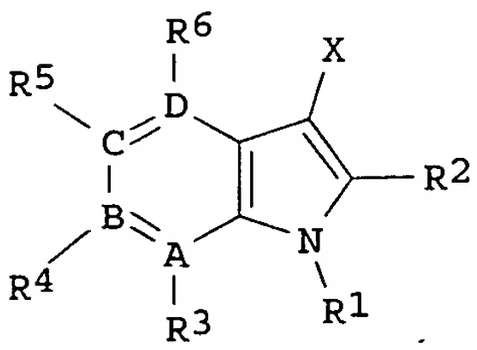
L24  ANSWER 1 OF 17  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:470314  HCAPLUS
```

DOCUMENT NUMBER: 144:495330
TITLE: Nanoparticulate compositions of tubulin inhibitors for treatment of resistant cancers and other diseases
INVENTOR(S): Papadopoulos, Pavlos; Doty, Mark; Kipp, James E.; Roessler, Berthold
PATENT ASSIGNEE(S): Baxter International Inc., USA; Baxter Healthcare S.A.; Raab, Gerhard
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006052712	A1	20060518	WO 2005-US39922	20051103
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006110462	A1	20060525	US 2005-266518	20051103

PRIORITY APPLN. INFO.: US 2004-626036P P 20041108
US 2005-642878P P 20050111

OTHER SOURCE(S): MARPAT 144:495330
ED Entered STN: 19 May 2006
GI



I

AB The present invention is directed to novel pharmaceutical compns. comprising nano- and micro-particulate formulations of poorly water soluble tubulin inhibitors (I; R1 = H, alkyl, alkylaryl, acyl, aryl; R2 = H, alkyl, acyl, aryl, alkoxycarbonyl, aryloxycarbonyl, cycloalkoxycarbonyl, etc.; R3-6 = H, alkyl, halogen; A,B,C,D = C, N; X = H, OH, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, acyl, carboxy, alkoxy, etc.). A tubulin inhibitor is preferably of the indole chemical class, N-substituted indol-3-glyoxyamides, and more preferably N-(pyridin-4-yl)-[1-(4-chlorobenzyl)-indol-3-yl]glyoxylic acid amide (D 24851, Indibulin). Methods of making and using such compns. for the treatment of anti-tumor agent resistant cancers and other diseases are also described. For example, a suspension of D-24851 was prepared by mixing an aqueous surfactant

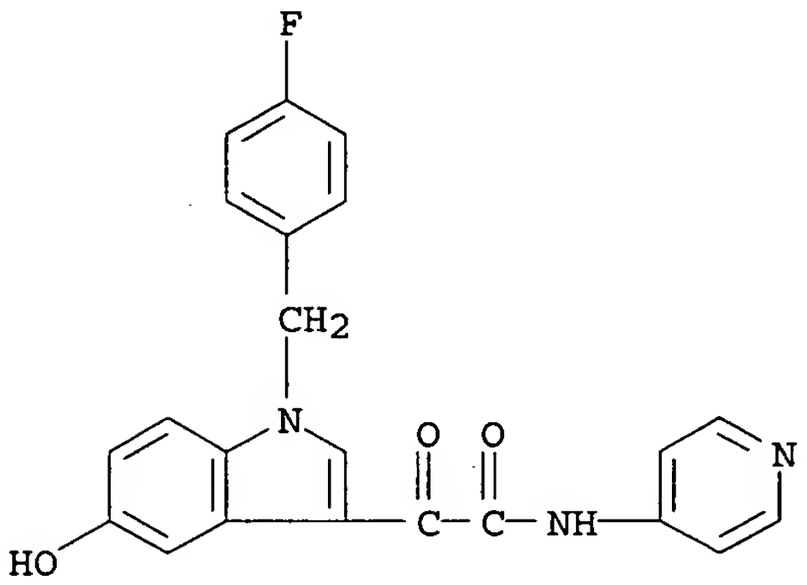
solution containing 0.1% sodium deoxycholate, 2.2% glycerin, and 0.142% dibasic sodium phosphate with a solution of D-24851 and Poloxamer 188 in lactic acid. The total suspension weight was 2000 g, with a drug concentration of approx. 1%.

The suspension was homogenized, lactic acid was removed and the suspension was homogenized again to give a nanosuspension with the mean particle size of approx. 325 nm.

IT **204206-02-0**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(particulate compns. of tubulin inhibitors for treatment of resistant cancers and other diseases)

RN 204206-02-0 HCAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:365169 HCAPLUS
DOCUMENT NUMBER: 144:419682
TITLE: Pharmaceutical compositions containing phosphodiesterase IV inhibitors and immunosuppressants
INVENTOR(S): Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko; Ohshima, Etsuo
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041120	A1	20060420	WO 2005-JP18854	20051013

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,

YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-299104 A 20041013
JP 2005-113265 A 20050411

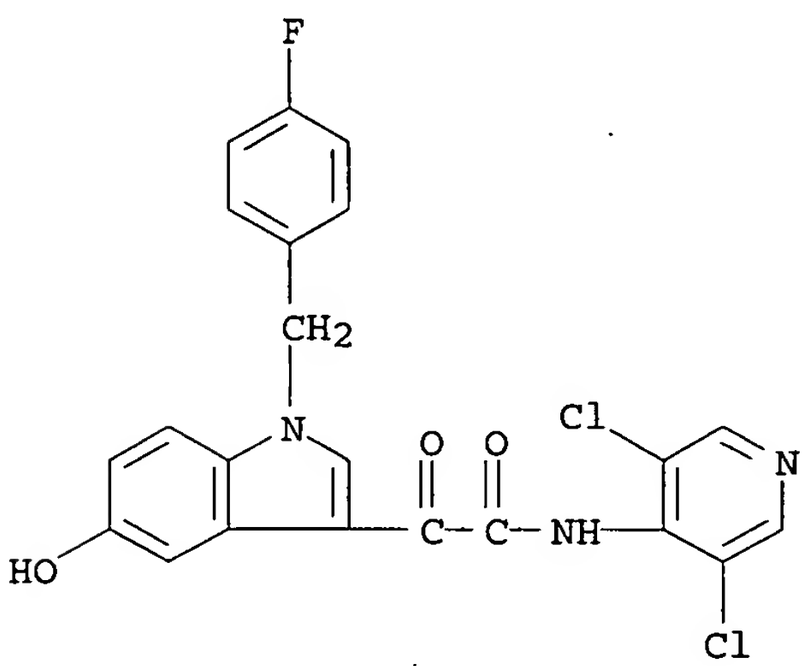
ED Entered STN: 21 Apr 2006

AB This invention relates to pharmaceutical compns. for the prevention and treatment of chronic **skin** diseases, comprising (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) an immunosuppressant, which are administered simultaneously or sep. with an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7-methoxyspiro[1,3-benzodioxole-2,1'-cyclopentan]-4-yl)ethanone (PDE-IV inhibitor) 20, tacrolimus (immunosuppressant) 20, lactose 123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

IT **257892-33-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase IV inhibitor and immunosuppressant combinations for treatment of chronic **skin** diseases)

RN 257892-33-4 HCAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:364924 HCAPLUS
DOCUMENT NUMBER: 144:398341
TITLE: Phosphodiesterase IV inhibitor and steroid combinations for the treatment of chronic **skin** disease
INVENTOR(S): Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko; Ohshima, Etsuo
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041121	A1	20060420	WO 2005-JP18855	20051013

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-299103 A 20041013
JP 2005-113264 A 20050411

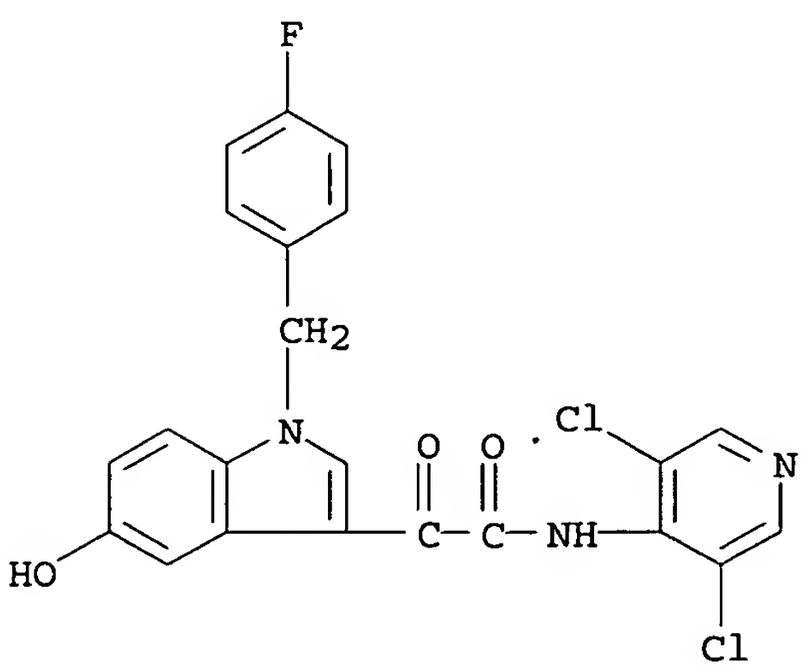
ED Entered STN: 21 Apr 2006

AB It is intended to provide a remedy and/or a preventive for a chronic **skin** disease which comprises (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) a steroid drug, which are administered simultaneously or sep. at an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7-methoxyspiro[1,3-benzodioxole-2,1'-cyclopentan]-4-yl)ethanone 50, prednisolone 20, lactose 123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase IV inhibitor and steroid combinations for treatment of chronic **skin** disease)

RN 257892-33-4 HCAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

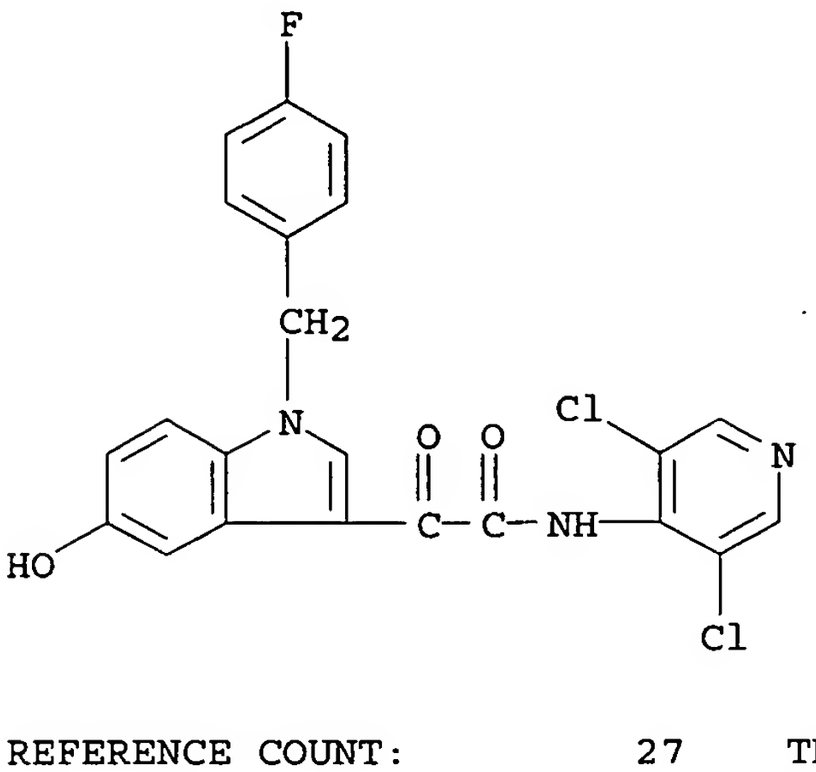


REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT .

L24 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:226501 HCAPLUS
DOCUMENT NUMBER: 144:267237
TITLE: The phosphodiesterase 4 inhibitor AWD 12-281 is active in a new guinea-pig model of allergic **skin** inflammation predictive of human **skin** penetration and suppresses both Th1 and Th2 cytokines in mice
AUTHOR(S): Hoppmann, Joachim; Baeumer, Wolfgang; Galetzka, Christin; Hoefgen, Norbert; Kietzmann, Manfred; Rundfeldt, Chris
CORPORATE SOURCE: Department of Pharmacology, elbion AG, Radebeul, D-01445, Germany
SOURCE: Journal of Pharmacy and Pharmacology (2005), 57(12), 1609-1617
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 Mar 2006
AB The selective phosphodiesterase 4 (PDE4) inhibitor AWD 12-281 is structurally optimized for topical administration. It has potent effects in models of lung inflammation if administered as a dry powder inhalation. It has also demonstrated its anti-inflammatory property in a mouse model of cutaneous inflammation after topical administration. The aim of this study was to evaluate whether AWD 12-281 may be capable of penetrating human **skin.** Therefore a new guinea-pig model of allergic **skin** inflammation had to be developed. In ovalbumin-sensitized guinea-pigs, intracutaneous administration of ovalbumin results in a rapid development of allergic **skin** wheals. Topically administered AWD 12-281 was capable of reducing the development of wheals, indicating that this compound can penetrate the stratum corneum of guinea-pig **skin** as a predictor of human **skin** penetration. A secondary aim was the evaluation of a T cell subtype preference of AWD 12-281 since PDE4 inhibitors are said to preferentially inhibit Th2-type cytokines. Therefore, the effects of AWD 12-281 on a broad spectrum of Th1- and Th2-type cytokines were studied in tissue homogenates after allergen challenge in sensitized mice and in supernatants of anti CD3/anti-CD28-stimulated peripheral blood mononuclear cells (PBMCs). In both models, AWD 12-281 suppressed both T cell subtype cytokines indicating a broad spectrum activity of AWD 12-281. A further issue was to determine the duration of action and the concentration-response relation of the topical activity of AWD 12-281 using a model of acute local inflammation - the arachidonic-acid-induced mouse ear edema. The compound exhibited a dose-dependent effect with a minimally effective concentration of 0.3%; after repeated administration the minimally effective concentration was 0.03%. A single administration of a 3% solution resulted in significant suppression of inflammation even 48 h after treatment. In conclusion, our results indicate that AWD 12-281 is a very promising drug candidate not only for the treatment of lung inflammation using inhalative administration but also for the treatment of atopic **dermatitis.**
IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 inhibitor AWD 12-281 is active in a new guinea-pig model of allergic **skin** inflammation predictive of human **skin** penetration and suppresses both Th1 and Th2 cytokines in

mice)
RN 257892-33-4 HCAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:149262 HCAPLUS
DOCUMENT NUMBER: 144:239931
TITLE: Pharmaceutical compositions for the treatment of respiratory and gastrointestinal disorders
INVENTOR(S): Jung, Birgit; Himmelsbach, Frank
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co. KG
SOURCE: PCT Int. Appl., 321 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015775	A2	20060216	WO 2005-EP8385	20050803
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006035893	A1	20060216	US 2005-189643	20050726

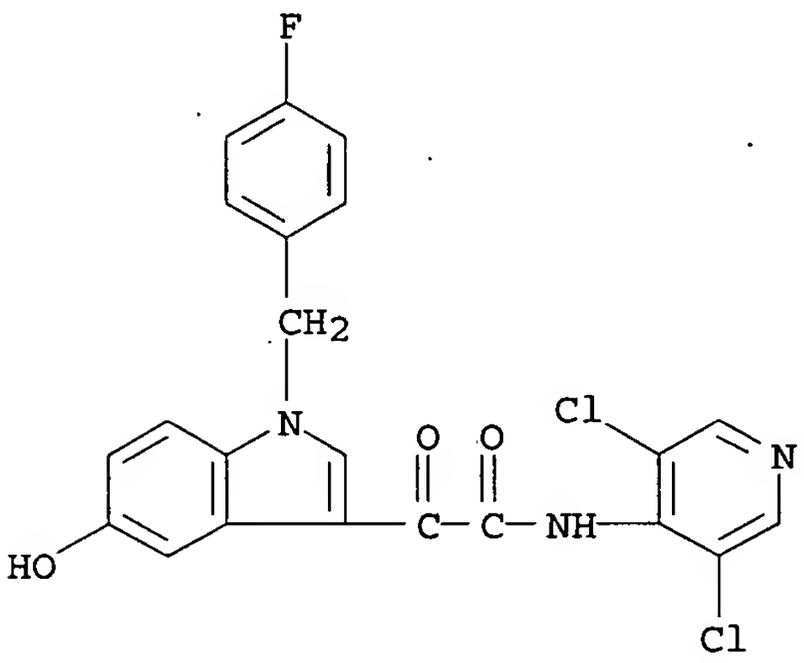
PRIORITY APPLN. INFO.: EP 2004-18808 A 20040807
OTHER SOURCE(S): MARPAT 144:239931
ED Entered STN: 17 Feb 2006

AB The present invention relates to novel pharmaceutical compns. comprising at least 1 EGFR kinase inhibitor and at least one addnl. active compound selected from β-2 mimetics, steroids, PDE-IV inhibitors, p38 MAP kinase inhibitors, NK1 antagonists and endothelin-antagonists, processes for preparing the compns. and the use thereof as drugs in the treatment of respiratory or gastrointestinal complaints, as well as inflammatory diseases of the joints, the **skin** or the eyes. Thus, an inhalable powder contained an EGFR kinase inhibitor 150, formoterol fumarate dihydrate 50, and lactose 12,300 mg/capsule.

IT **257892-33-4**, AWD 12-281
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for treatment of respiratory and gastrointestinal disorders)

RN 257892-33-4 HCAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L24 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1155523 HCAPLUS
DOCUMENT NUMBER: 143:416252
TITLE: Novel medicament combinations for the treatment of respiratory diseases
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

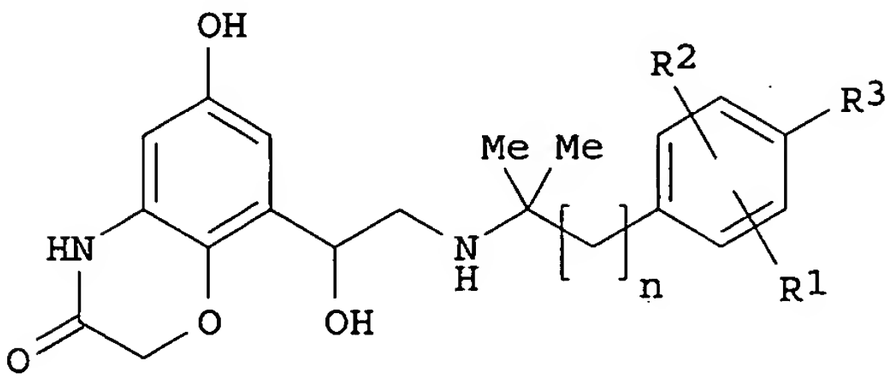
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005239778	A1	20051027	US 2005-109094	20050419
DE 102004019540	A1	20051110	DE 2004-102004019540	20040422
DE 102004052987	A1	20060504	DE 2004-102004052987	20041103
WO 2005102349	A1	20051103	WO 2005-EP4073	20050418

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,

SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2004-102004019540A 20040422
US 2004-578542P P 20040610
DE 2004-102004052987A 20041103
EP 2005-2496 A 20050207

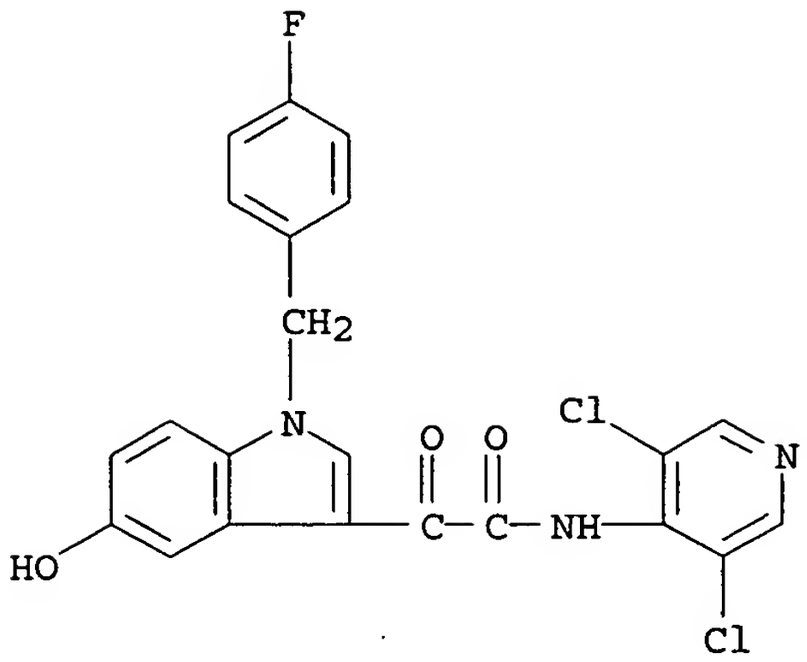
OTHER SOURCE(S): MARPAT 143:416252
ED Entered STN: 28 Oct 2005
GI



I

AB The present invention relates to a pharmaceutical composition comprising one or more compds. of formula I wherein n denotes 1 or 2; R1 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R2 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R3 denotes C1-C4-alkyl, OH, halogen, -O-C1-C4-alkyl, -O-C1-C4-alkylene-COOH, -O-C1-C4-alkylene-CO-O-C1-C4-alkyl, and at least one other active substance for the treatment of respiratory diseases. The second active substance can by an anticholinergic, a phosphodiesterase IV inhibitor, a steroid, a LTD4 antagonist or an EGFR inhibitor.

IT **257892-33-4**, AWD-12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase IV inhibitor; novel medicament combinations for treatment of respiratory diseases)
RN 257892-33-4 HCAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

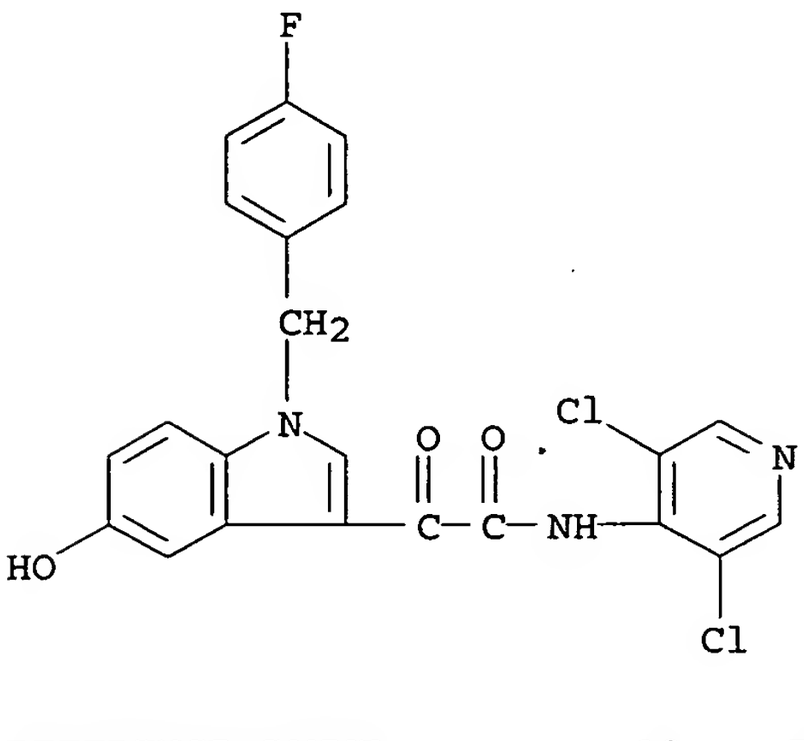


L24 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:467725 HCAPLUS
DOCUMENT NUMBER: 141:17651
TITLE: Phosphodiesterase IV and phosphodiesterase III/IV inhibitors for use in the treatment of cachexia
INVENTOR(S): Schmidt, Mathias
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047817	A1	20040610	WO 2003-EP13313	20031126
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, EG, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2506949	AA	20040610	CA 2003-2506949	20031126
AU 2003289898	A1	20040618	AU 2003-289898	20031126
EP 1567136	A1	20050831	EP 2003-782232	20031126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006508996	T2	20060316	JP 2004-554493	20031126
US 2006079540	A1	20060413	US 2005-535815	20050520
PRIORITY APPLN. INFO.:			EP 2002-26548 A	20021127
			WO 2003-EP13313 W	20031126

ED Entered STN: 10 Jun 2004
AB The invention discloses the use of a PDE IV or PDE III/IV inhibitor for the treatment of cachexia.
IT **257892-33-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase IV and phosphodiesterase III/IV inhibitors for treatment of cachexia)
RN 257892-33-4 HCAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



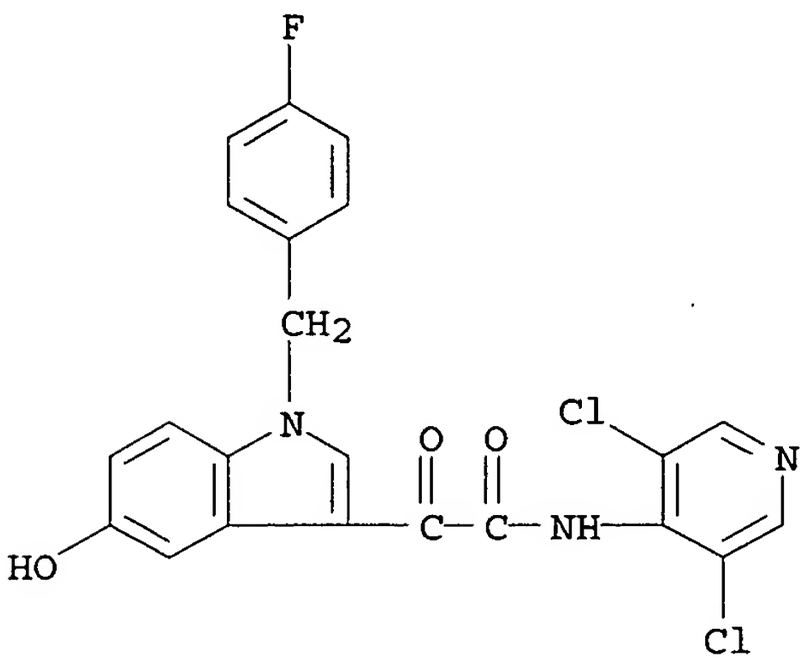
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:60309 HCAPLUS
DOCUMENT NUMBER: 140:105273
TITLE: Topical treatment of **skin** diseases
INVENTOR(S): Rundfeldt, Chris; Kietzmann, Manfred; Hoppmann, Joachim; Baeumer, Wolfgang; Kuss, Hildegard; Hoefgen, Norbert
PATENT ASSIGNEE(S): Elbion AG, Germany
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006920	A1	20040122	WO 2003-EP7514	20030710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004038958	A1	20040226	US 2003-611649	20030701
CA 2492093	AA	20040122	CA 2003-2492093	20030710
AU 2003254332	A1	20040202	AU 2003-254332	20030710
BR 2003012696	A	20050426	BR 2003-12696	20030710
EP 1531818	A1	20050525	EP 2003-763810	20030710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1681500	A	20051012	CN 2003-821520	20030710

JP 2005537262	T2	20051208	JP 2004-520586		20030710
ZA 2005000108	A	20050223	ZA 2005-108		20050106
NO 2005000718	A	20050401	NO 2005-718		20050210
PRIORITY APPLN. INFO.:			US 2002-395221P	P	20020711
			WO 2003-EP7514	W	20030710

OTHER SOURCE(S): MARPAT 140:105273
ED Entered STN: 26 Jan 2004
AB The present invention relates to a method for the treatment of an inflammatory and/or allergic **skin** disease comprising topically administering a substituted hydroxy indole which is a phosphodiesterase 4 inhibitor. Examples are provided of the topical effectiveness of AWD 12-281 and cilomilast in **dermal** immunol. inflammation.
IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitors for treatment of **skin** inflammatory and/or allergic reactions)
RN 257892-33-4 HCAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



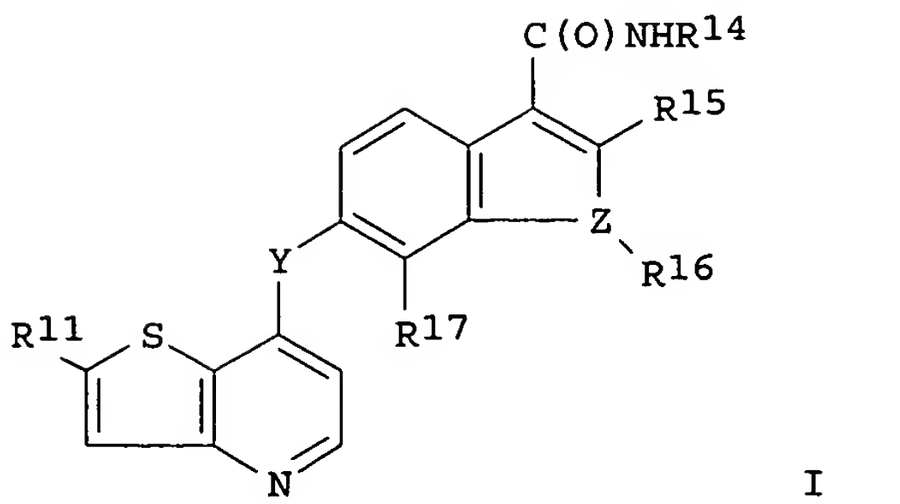
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

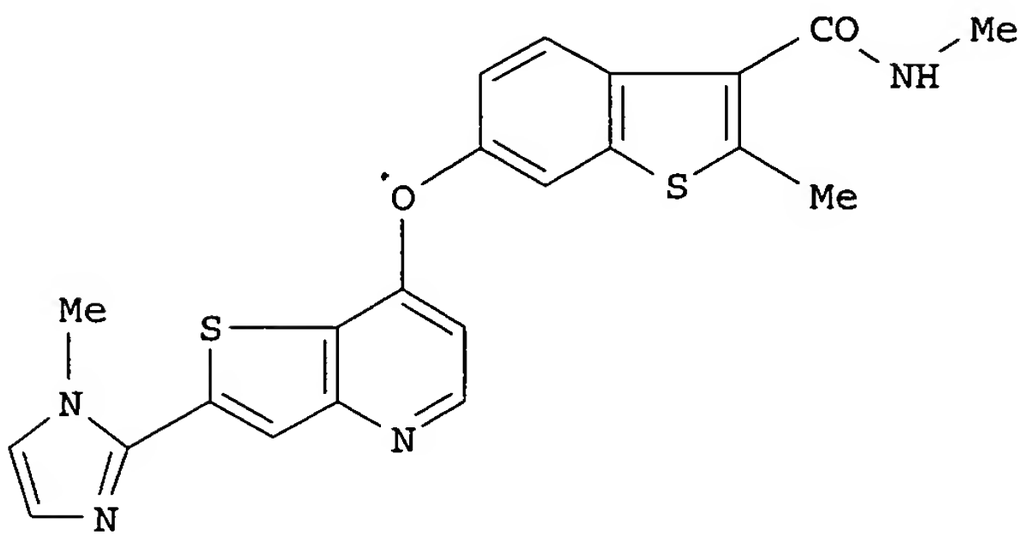
ACCESSION NUMBER:	2003:1006988 HCAPLUS
DOCUMENT NUMBER:	140:59632
TITLE:	Preparation of benzofused heteroaryl amide derivatives of thienopyridines as tyrosine kinase inhibitors useful against hyperproliferative disorders
INVENTOR(S):	Romines, William Henry, III; Kania, Robert Steven; Lou, Jihong; Collins, Michael Raymond; Cripps, Stephan James; He, Mingying; Zhou, Ru; Palmer, Cynthia Louise; Deal, Judith Gail
PATENT ASSIGNEE(S):	Pfizer Inc., USA
SOURCE:	PCT Int. Appl., 194 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003106462	A1	20031224	WO 2003-IB2393		20030604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2489466	AA	20031224	CA 2003-2489466		20030604
AU 2003233134	A1	20031231	AU 2003-233134		20030604
EP 1515975	A1	20050323	EP 2003-727888		20030604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003011806	A	20050329	BR 2003-11806		20030604
CN 1671714	A	20050921	CN 2003-818109		20030604
JP 2005534669	T2	20051117	JP 2004-513293		20030604
US 2004009965	A1	20040115	US 2003-460010		20030611
US 6869962	B2	20050322			
US 2004186126	A1	20040923	US 2004-796226		20040309
US 7045528	B2	20060516			
NO 2004005103	A	20050217	NO 2004-5103		20041124
US 2006079548	A1	20060413	US 2005-256477		20051021
PRIORITY APPLN. INFO.:			US 2002-389110P	P	20020614
			WO 2003-IB2393	W	20030604
			US 2003-460010	A3	20030611
			US 2004-796226	A1	20040309

OTHER SOURCE(S): MARPAT 140:59632
ED Entered STN: 26 Dec 2003
GI



I



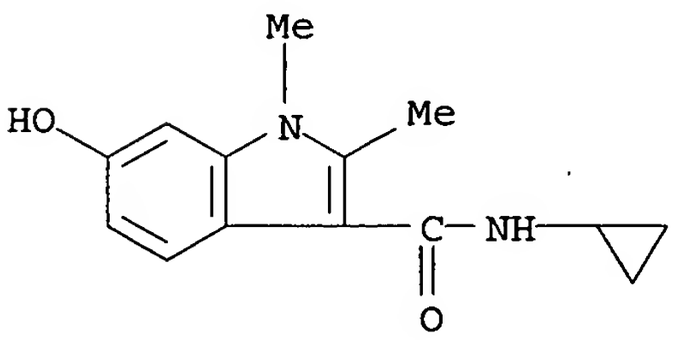
II

AB The invention relates to benzofused heteroaryl amide derivs. of thienopyridines (shown as I; variables defined below; e.g. II) and to prodrugs or metabolites thereof, or pharmaceutically acceptable salts or solvates of said compds., prodrugs, and metabolites. The invention also relates to pharmaceutical compns. containing I and to methods of treating hyperproliferative disorders in a mammal by administering I. Inhibitory activities of >200 examples of I are tabulated for a number of tyrosine kinases. Also, pharmacokinetics of 19 examples of I in mice and metabolism in human liver microsomes were analyzed. Although the methods of preparation are not claimed, 140 example prepns. are included. For example, II was prepared in 5 steps starting from 3-methoxybenzenethiol and bromoacetaldehyde di-Et acetal and involving intermediates 1-[(2,2-diethoxyethyl)sulfanyl]-3-methoxybenzene, 6-methoxy-2-methylbenzo[b]thiophene, 6-methoxy-2-methylbenzo[b]thiophene-3-carboxylic acid methylamide, and 6-hydroxy-2-methylbenzo[b]thiophene-3-carboxylic acid methylamide; the last step comprises reaction of 7-chloro-2-(1-methyl-1H-imidazol-2-yl)thieno[3,2-b]pyridine and 6-hydroxy-2-methylbenzo[b]thiophene-3-carboxylic acid methylamide (40 %). For I: Y is NH, O, S, or CH2; Z is O, S, or N; R14 is a C1-C6 alkyl, C1-C6 alkylamino, C1-C6 alkylhydroxy, C3-C10 cycloalkylamino, or methylureido group; R15 and R17 = H, halo, or a C1-C6 alkyl group (un)substituted by ≥1 R5 groups. R16 is H or a C1-C6 alkyl group when Z is N, and R16 is absent when Z is O or S; R11 is H, C1-C6 alkyl, C3-C10 cycloalkyl, C(O)NR12R3, C(O)(C6-C10 aryl), (CH2)t(C6-C10 aryl), (CH2)t(5 to 10 membered heterocyclic), (CH2)tNR12R13, SO2NR12R13 or CO2R12. Each R5 = halo, cyano, nitro, trifluoromethoxy, trifluoromethyl, azido, C(O)R8, C(O)OR8, OC(O)R8, OC(O)OR8, NR6C(O)R7, C(O)NR6R7, NR6R7, OR9, SO2NR6R7, C1-C6 alkyl, C3-C10 cycloalkyl, C1-C6 alkylamino, (CH2)jO(CH2)qNR6R7, (CH2)tO(CH2)qOR9, (CH2)tOR9, S(O)j(C1-C6 alkyl), (CH2)t(C6-C10 aryl), (CH2)t(5 to 10 membered heterocyclic), C(O)(CH2)t(C6-C10 aryl), (CH2)tO(CH2)j(C6-C10 aryl), (CH2)tO(CH2)q(5 to 10 membered heterocyclic), C(O)(CH2)t(5 to 10 membered heterocyclic), (CH2)jNR7(CH2)qN R6R7, (CH2)jNR7CH2C(O)NR6R7, (CH2)jNR7(CH2)qNR9C(O)R8,

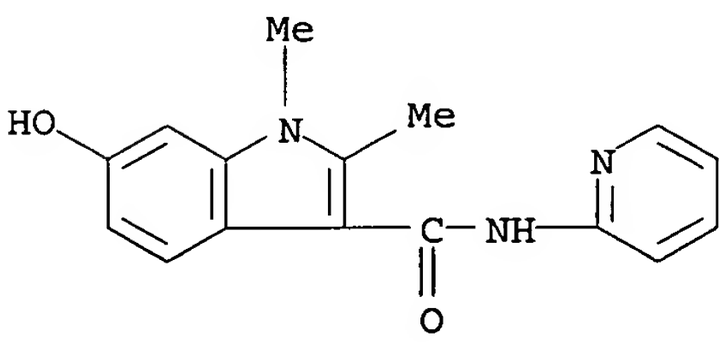
(CH2)jNR7(CH2)tO(CH2)qOR9, (CH2)jNR7(CH2)qS(O)j(C1-C6 alkyl), (CH2)jNR7(CH2)tR6, SO2(CH2)t(C6-C10 aryl), and SO2(CH2)t(5 to 10 membered heterocyclic). Each R6 and R7 = H, OH, C1-C6 alkyl, C3-C10 cycloalkyl, (CH2)t(C6-C10 aryl), (CH2)t(5 to 10 membered heterocyclic), (CH2)tO(CH2)qOR9, (CH2)tCN(CH2)tOR9, (CH2)tCN(CH2)tR9 and (CH2)tOR9; each R8 = H, C1-C10 alkyl, C3-C10 cycloalkyl, (CH2)t(C6-C10 aryl), and (CH2)t(5 to 10 membered heterocyclic); t = 0-6; j = 0-2; q = 2-6; each R9 and R10 = H, OR6, C1-C6 alkyl, and C3-C10 cycloalkyl. Each R12 and R13 = H, C1-C6 alkyl, C3-C10 cycloalkyl, (CH2)t(C3-C10 cycloalkyl), (CH2)t(C6-C10 aryl), (CH2)t(5 to 10 membered heterocyclic), (CH2)tO(CH2)qOR9, and (CH2)tOR9; addnl. details including provisos are given in the claims.

IT **638217-26-2P 638218-20-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzofused heteroaryl amide derivs. of thienopyridines as tyrosine kinase inhibitors useful against hyperproliferative disorders)

RN 638217-26-2 HCAPLUS
CN 1H-Indole-3-carboxamide, N-cyclopropyl-6-hydroxy-1,2-dimethyl- (9CI) (CA INDEX NAME)



RN 638218-20-9 HCAPLUS
CN 1H-Indole-3-carboxamide, 6-hydroxy-1,2-dimethyl-N-2-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

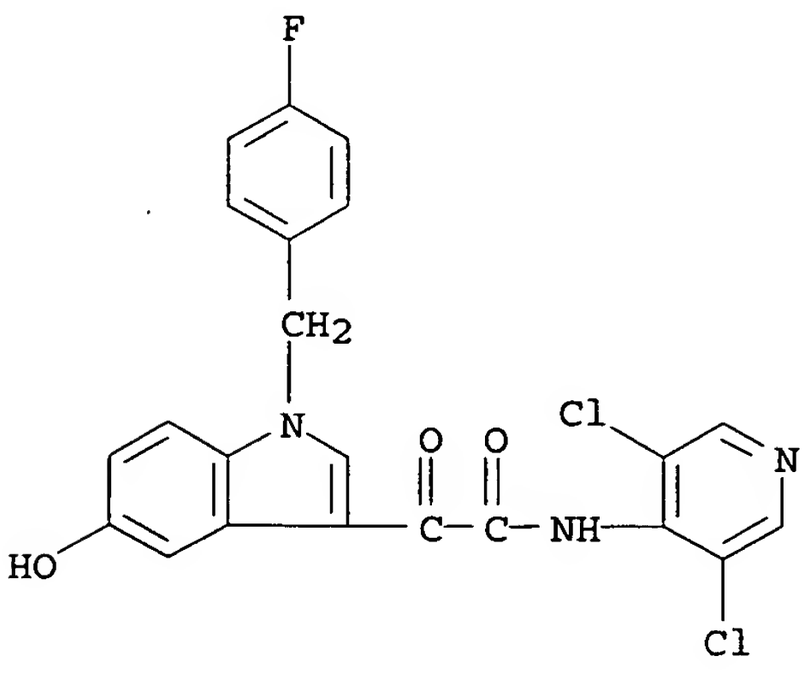
L24 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:695438 HCAPLUS
DOCUMENT NUMBER: 140:87294
TITLE: AWD 12-281, a highly selective phosphodiesterase 4 inhibitor, is effective in the prevention and treatment of inflammatory reactions in a model of allergic **dermatitis**
AUTHOR(S): Baeumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Rundfeldt, Chris; Kietzmann, Manfred
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy,

School of Veterinary Medicine, Hannover, D-30559, Germany
SOURCE: Journal of Pharmacy and Pharmacology (2003), 55(8), 1107-1114
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Sep 2003

AB AWD 12-281 (N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide), a phosphodiesterase 4 inhibitor, which is optimized for topical administration, was tested in a model of allergic **dermatitis** in mice. To obtain an allergic **dermatitis**, BALB/c mice were sensitized to toluene-2,4-diisocyanate (TDI). The allergic reaction was challenged by topical administration of TDI onto the mice ears. AWD 12-281 was tested for its anti-inflammatory potential by oral, i.p. and topical administration. The phosphodiesterase 4 inhibitor, cilomilast (SB 207499), and/or the corticosteroid, diflorasone diacetate, were used as reference compds. Given orally and i.p. 2 h before as well as 5 and 24 h after TDI challenge, AWD 12-281 showed no, or only a transient inhibition of the allergen-induced ear swelling, whereas cilomilast significantly inhibited this ear swelling. Applied topically onto the ears before TDI challenge, AWD 12-281, cilomilast and diflorasone diacetate caused total inhibition of ear swelling 24 h after challenge, confirmed by a decrease of the pro-inflammatory cytokines interleukin-4, interleukin-6 and macrophage inhibitory protein-2. Administered topically after TDI challenge as therapeutic intervention, AWD 12-281 and diflorasone diacetate caused significant inhibition of ear swelling; cilomilast failed to do so. These results indicate that topically administered AWD 12-281 may be potent in the prevention and treatment of allergic/inflammatory **skin** diseases.

IT **257892-33-4**, AWD 12-281
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AWD 12-281, a highly selective phosphodiesterase 4 inhibitor, is effective in prevention and treatment of inflammatory reactions in a model of allergic **dermatitis**)

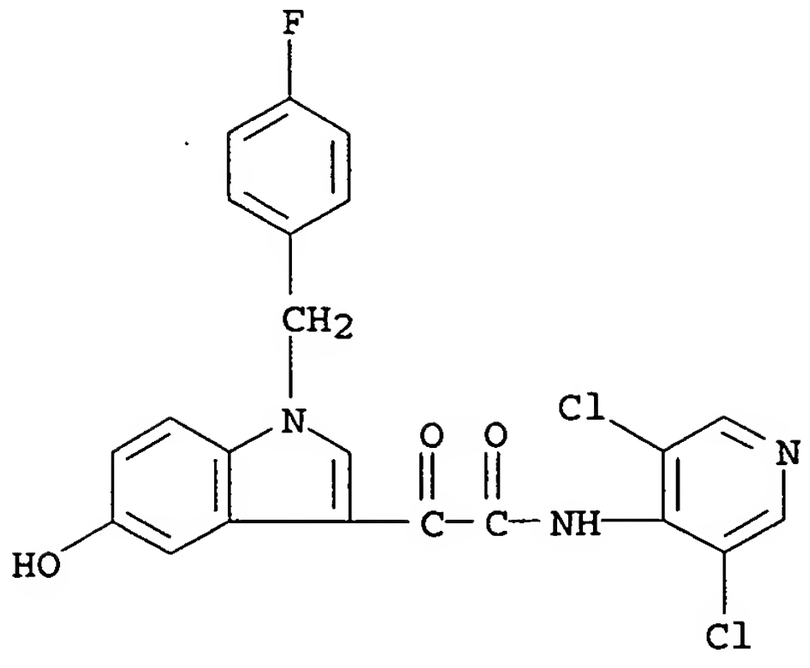
RN 257892-33-4 HCAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:495906 HCAPLUS
DOCUMENT NUMBER: 138:117605
TITLE: Effects of the phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on the inflammatory reaction in a model of allergic **dermatitis**
AUTHOR(S): Baumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Ehinger, Britt; Kietzmann, Manfred
CORPORATE SOURCE: Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hanover, 30559, Germany
SOURCE: European Journal of Pharmacology (2002), 446(1-3), 195-200
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Jul 2002
AB The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast, c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were tested in a model of allergic **dermatitis** in mice. To obtain an allergic **dermatitis**, BALB/c mice were sensitized to toluene-2,4-diisocyanate. The allergic reaction was challenged by topical administration of toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups of mice were treated topically (ear **skin**) with SB 207499 or AWD 12-281. There was a significant ear swelling in toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after challenge. SB 207499 and AWD 12-281 inhibited this swelling significantly 8, 16, 24 and 48 h after the challenge. For biochem. parameters and histol., ears were sampled from mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue, SB 207499 and AWD 12-281 inhibited significantly the secretion of interleukin 1β induced by toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx (granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and 16 h after challenge was nearly abolished by AWD 12-281 and SB 204799.
IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on inflammatory reaction in a model of allergic **dermatitis**)
RN 257892-33-4 HCAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

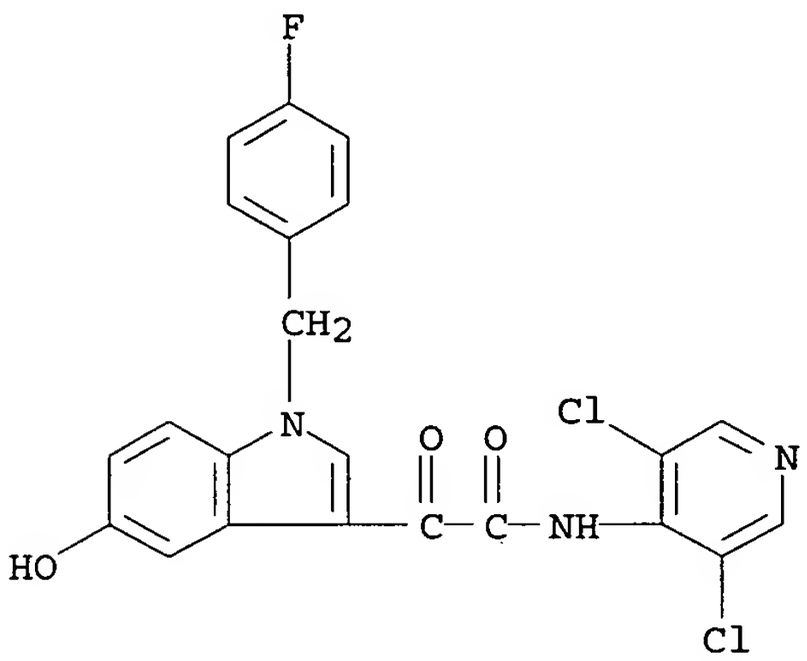
L24 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:30560 HCAPLUS
DOCUMENT NUMBER: 134:221365
TITLE: The effect of selective and non-selective phosphodiesterase inhibitors on allergen- and leukotriene C4-induced contractions in passively sensitized human airways
AUTHOR(S): Schmidt, Dunja T.; Watson, Nikki; Dent, Gordon; Ruhlmann, Elke; Branscheid, Detlev; Magnussen, Helgo; Rabe, Klaus F.
CORPORATE SOURCE: Department of Pulmonology, Leiden University Medical Centre, Leiden, NL-2333 ZA, Neth.
SOURCE: British Journal of Pharmacology (2000), 131(8), 1607-1618
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Jan 2001
AB Non-selective inhibitors of cyclic nucleotide phosphodiesterase (PDE) block allergen-induced contraction of passively sensitized human airways in vitro by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of histamine and cysteinyl leukotriene (LT) release from airways. We investigated the effects of non-selective PDE inhibitors and selective inhibitors of PDE3 and PDE4 in order to determine the involvement of PDE isoenzymes in the suppression of allergic bronchoconstriction. Macroscopically normal airways from 76 patients were sensitized with IgE-rich sera (>250 u ml-1) containing specific antibodies against allergen (**Dermatophagoides** farinae). Contractile responses of bronchial rings were assessed using standard organ bath techniques. Passive sensitization caused increased contractile responses to allergen, histamine and LTC4. Non-selective PDE inhibitors (theophylline, 3-isobutyl-1-methylxanthine [IBMX]), a PDE3-selective inhibitor (motapizone), PDE4-selective inhibitors (RP73401, rolipram, AWD 12-281) and a mixed PDE3/4 inhibitor (zardaverine) all significantly relaxed inherent bronchial tone at resting tension and to a similar degree. Theophylline, IBMX, zardaverine and the combination of motapizone and RP73401 inhibited the contractile responses to allergen and LTC4. Pre-treatment with motapizone, RP73401, rolipram or the methylxanthine

adenosine receptor antagonist, 8-phenyltheophylline, did not significantly decrease responses to either allergen or LTC4. We conclude that combined inhibition of PDE3 and PDE4, but not selective inhibition of either isoenzyme or antagonism of adenosine receptors, is effective in suppressing allergen-induced contractions of passively sensitized human airways. The relationship between allergen- and LTC4-induced responses suggests that PDE inhibitors with PDE3 and PDE4 selectivity are likely to act in part through inhibition of mediator release and not simply through direct relaxant actions on airway smooth muscle.

IT **257892-33-4**, AWD 12-281
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phosphodiesterase inhibitors in allergen- and leukotriene C4-induced contractions in sensitized human airways)

RN 257892-33-4 HCAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

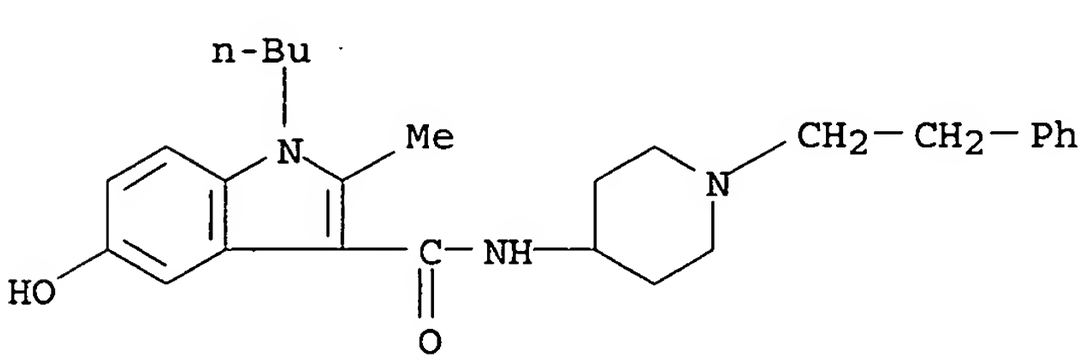
L24 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:562996 HCAPLUS
DOCUMENT NUMBER: 127:239123
TITLE: Combinations having immunosuppressive effects, containing cyclooxygenase-2-inhibitors and 5-lipoxygenase inhibitors
INVENTOR(S): Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729776	A1	19970821	WO 1997-US1558	19970212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,				

LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG

CA 2246265	AA	19970821	CA 1997-2246265		19970212
AU 9718505	A1	19970902	AU 1997-18505		19970212
EP 888127	A1	19990107	EP 1997-904133		19970212
EP 888127	B1	20011212			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 2000504723	T2	20000418	JP 1997-529363		19970212
AT 210461	E	20011215	AT 1997-904133		19970212
PT 888127	T	20020531	PT 1997-904133		19970212
ES 2169351	T3	20020701	ES 1997-904133		19970212
US 6376528	B1	20020423	US 1999-430072		19991018
US 2002143033	A1	20021003	US 2002-98644		20020315
PRIORITY APPLN. INFO.:			US 1996-600622	A1	19960213
			WO 1997-US1558	W	19970212
			US 1998-189463	B1	19981110
			US 1999-430072	A3	19991018

OTHER SOURCE(S): MARPAT 127:239123
ED Entered STN: 04 Sep 1997
AB Treatment with a cyclooxygenase-2 inhibitor and a 5-lipoxygenase inhibitor is described as being useful in reducing recipient rejection of transplanted organs and for treatment of autoimmune diseases. 4-[5-(3-Fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide and N'-[3-[5-(4-fluorophenoxy)-2-furyl]-1-methyl-2-propynyl]-N'-hydroxyurea were prepared and a combination of these 2 compds. showed a delay in rejection time of **skin** grafts while treatment alone of each of these compds. resulted in no prolongation of graft survival.
IT **130838-15-2**, Y-19432
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 and 5-lipoxygenase inhibitor combinations with immunosuppressive effects)
RN 130838-15-2 HCAPLUS
CN 1H-Indole-3-carboxamide, 1-butyl-5-hydroxy-2-methyl-N-[1-(2-phenylethyl)-4-piperidinyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

L24 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:994335 HCAPLUS
DOCUMENT NUMBER: 124:86811
TITLE: Novel indole derivatives useful to treat

estrogen-related neoplasms and disorders

INVENTOR(S): Bitonti, Alan J.; McDonald, Ian A.; Salituro, Francesco G.; Whitten, Jeffrey P.; Jarvi, Esa T.; Wright, Paul S.

PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

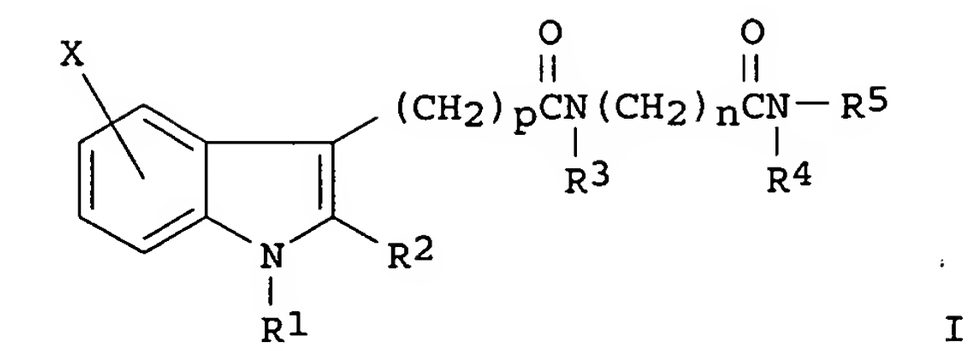
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522524	A1	19950824	WO 1995-US1372	19950131
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2183731	AA	19950824	CA 1995-2183731	19950131
CA 2183731	C	20000321		
AU 9518373	A1	19950904	AU 1995-18373	19950131
AU 680740	B2	19970807		
EP 746544	A1	19961211	EP 1995-910164	19950131
EP 746544	B1	19980909		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1141627	A	19970129	CN 1995-191750	19950131
HU 76133	A2	19970630	HU 1996-2299	19950131
JP 09509169	T2	19970916	JP 1995-521822	19950131
JP 3536258	B2	20040607		
AT 170839	E	19980915	AT 1995-910164	19950131
ES 2122555	T3	19981216	ES 1995-910164	19950131
ZA 9501297	A	19951024	ZA 1995-1297	19950216
US 5877202	A	19990302	US 1996-594505	19960131
FI 9603272	A	19960821	FI 1996-3272	19960821
NO 9603483	A	19961022	NO 1996-3483	19960821
PRIORITY APPLN. INFO.:			US 1994-200057 A2	19940222
			US 1994-362046 A2	19941222
			WO 1995-US1372 W	19950131

OTHER SOURCE(S): MARPAT 124:86811

ED Entered STN: 22 Dec 1995

GI



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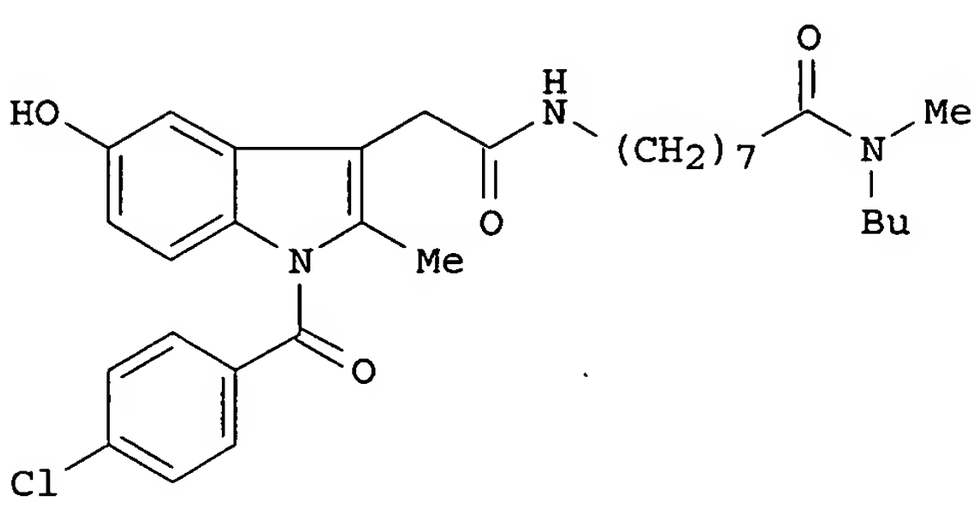


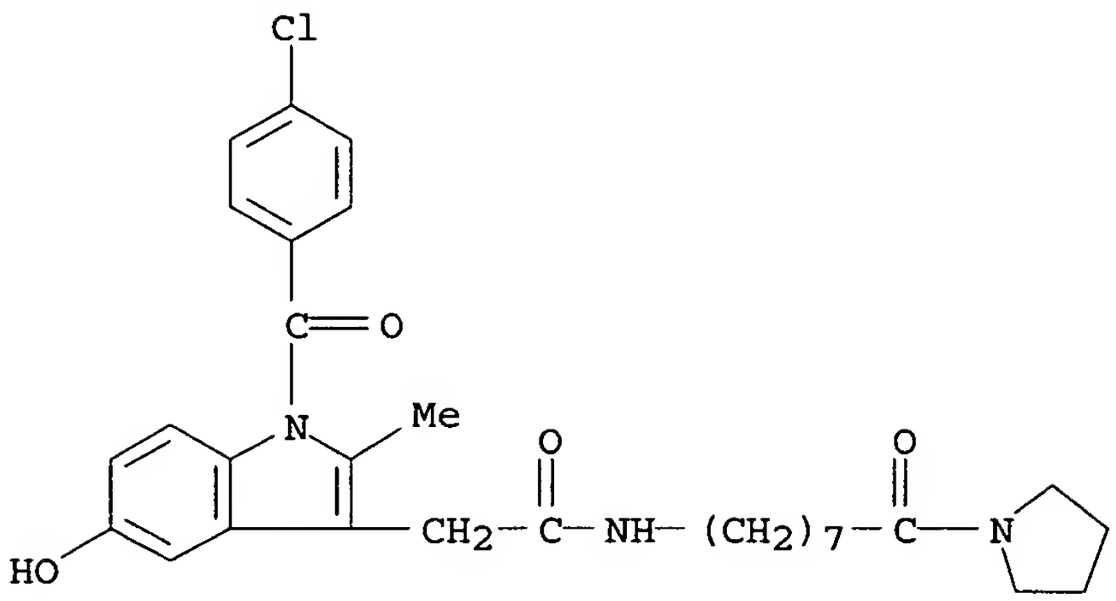
II

AB The invention relates to indole derivs. I [n = 1-12; p = 0, 1; X = 1-3 of H, halo, OH, alkyl, alkoxy, R6CO2; R1 = H, alkyl, (un)substituted phenylalkyl, benzoyl, carbamoyl, etc.; R2 = H, alkyl, (un)substituted Ph; R3, R4 = H, alkyl; R5 = H, alkyl, Ph; or R4R5 = CH2CH2GCH2CH2; G = bond, NMe, CH2, O; R6 = alkyl, (un)substituted Ph; one of R1-R5 ≠ H when n = 1] and their pharmaceutically acceptable salts. I and salts are useful in down-regulating estrogen receptor expression. Also included are methods for the treatment or prophylaxis of neoplasms or of controlling neoplasm growth, especially estrogen-dependent neoplasms such as those associated with breast, ovarian, and cervical tissue. Also provided is a method for treating autoimmune diseases. For example, reaction of 1-[5-methoxy-1-(4-chlorobenzoyl)-2-methyl-1H-indol-3-yl]acetic acid chloride with 8-aminooctanoic acid methylbutylamide [prepns. given] in PhMe in the presence of (iso-Pr)2NEt, and demethylation of the phenolic Me ether with BBr3 in CH2Cl2, gave the preferred compound II [also named MDL 101,906]. The latter inhibited estradiol-dependent transcription of an estradiol-dependent luciferase reporter plasmid in MCF-7 human breast tumor cells with an IC50 of 5.2 μM. Over 180 synthetic examples cover preparation of I and intermediates, and 9 biol. examples cover a variety of tests of selected I, including relative binding affinities to estrogen receptor, depletion of receptor from tumor cells, and inhibition of cells including tamoxifen-resistant LY-2 cells (IC50 of II = 4.7 μM).

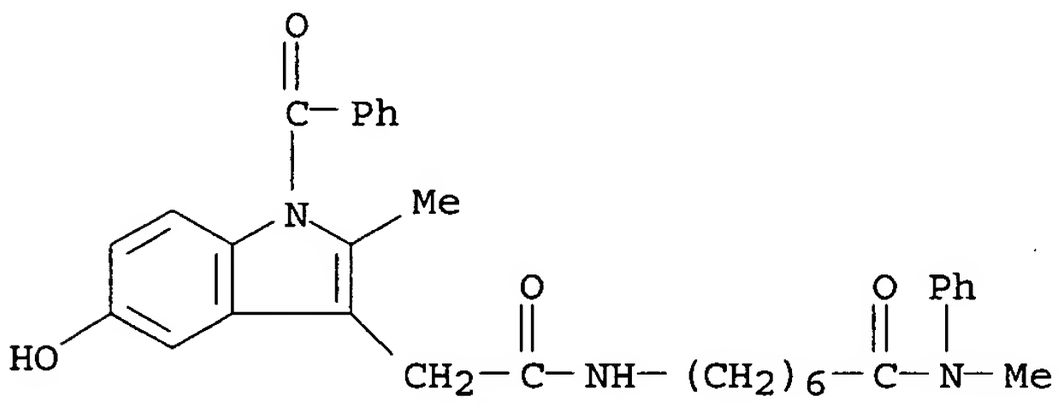
IT **172595-95-8P 172596-03-1P 172596-18-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indoles as estrogen-dependent antineoplastics)

RN 172595-95-8 HCAPLUS

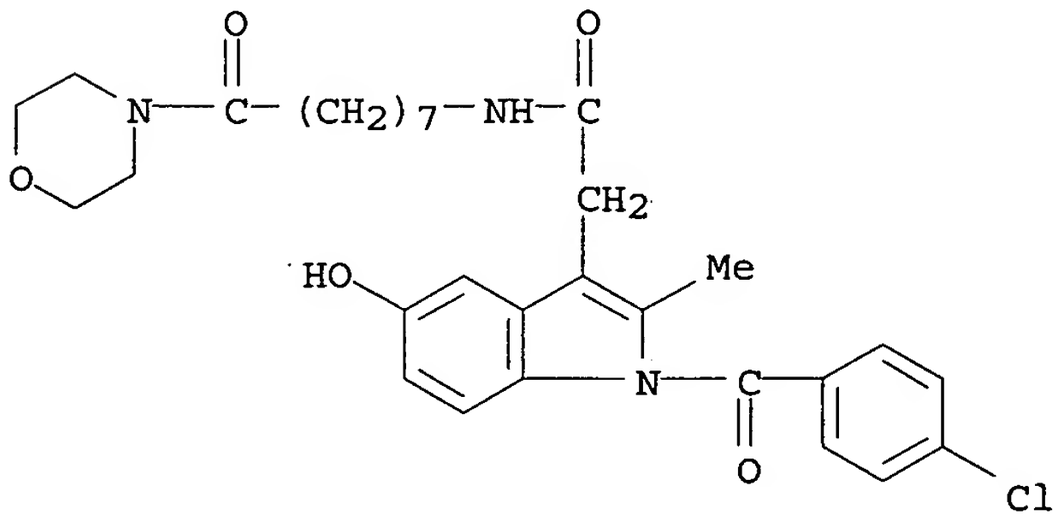
CN 1H-Indole-3-acetamide, 1-(4-chlorobenzoyl)-5-hydroxy-2-methyl-N-[8-oxo-8-(1-pyrrolidinyl)octyl]- (9CI) (CA INDEX NAME)



RN 172596-03-1 HCAPLUS
CN 1H-Indole-3-acetamide, 1-benzoyl-5-hydroxy-2-methyl-N-[7-(methylphenylamino)-7-oxoheptyl]- (9CI) (CA INDEX NAME)



RN 172596-18-8 HCAPLUS
CN 1H-Indole-3-acetamide, 1-(4-chlorobenzoyl)-5-hydroxy-2-methyl-N-[8-(4-morpholinyl)-8-oxooctyl]- (9CI) (CA INDEX NAME)

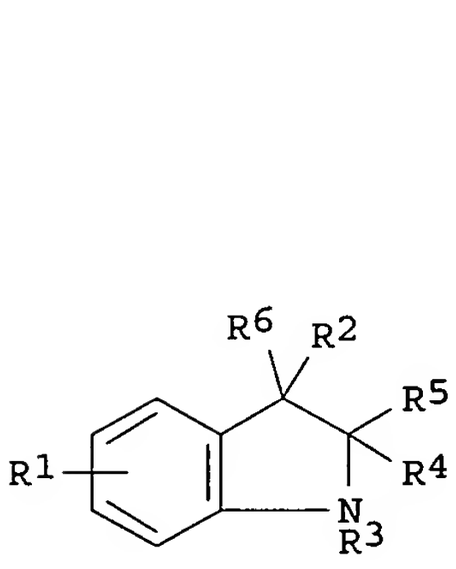


L24 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:982654 HCAPLUS
DOCUMENT NUMBER: 124:175826
TITLE: Preparation of 2-indolyldisulfides and analogs as protein tyrosine kinase inhibitors and antitumor agents
INVENTOR(S): Dobrusin, Ellen M.; Showalter, Howard D. H.; Denny, William A.; Palmer, Brian D.; Rewcastle, Gordon W.;

PATENT ASSIGNEE(S): Tercel, Moana; Thompson, Andrew M.
Warner-Lambert Co., USA
SOURCE: U.S., 53 pp. Cont.-in-part of U.S. Ser. No. 926, 015, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5464861	A	19951107	US 1993-94792		19930809
HU 71553	A2	19951228	HU 1995-341		19930802
CZ 283965	B6	19980715	CZ 1995-288		19930802
NZ 255194	A	20000128	NZ 1993-255194		19930802
US 5556874	A	19960917	US 1995-438616		19950510
PRIORITY APPLN. INFO.:			US 1992-926015	B2	19920806
			US 1993-94792	A3	19930809

OTHER SOURCE(S): MARPAT 124:175826
ED Entered STN: 14 Dec 1995
GI



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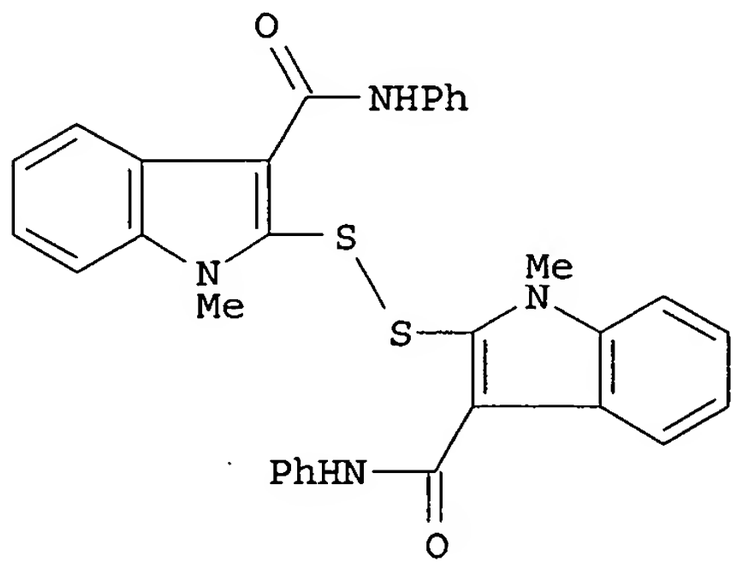
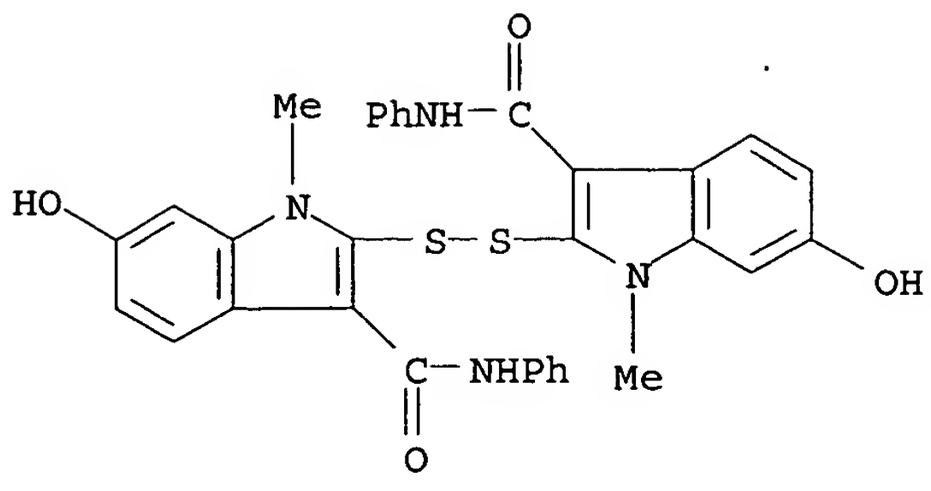


II

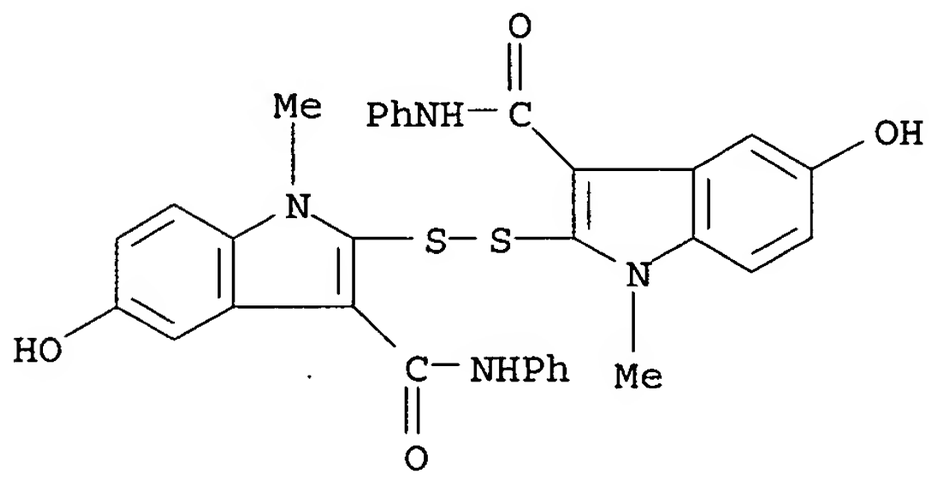
AB Title compds. [I; R1 = H, halo, alkyl, alkoxy, etc.; R2 = (acyl)alkyl, acyl, CH:CHCO2H, etc.; R3 = H, alkyl, CH2Ph; R4 = SH, SnR, SeH, SenR, etc.; R = H, alkyl, (hetero)aryl, I in which R4 = bond, etc.; R4R5 = S, Se; R5R6 = bond; R6 = H; n = 1-3] were prepared 2Hus, 1-methyl-2-indolinone was treated with P2S5 and the product condensed with PhNCO to give, after oxidation, title compound II which had IC50 of 3-4μM against growth factor mediated mitogenesis in vitro.

IT **158719-27-8P 158719-43-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-indolyldisulfides and analogs as protein tyrosine kinase inhibitors and antitumor agents)

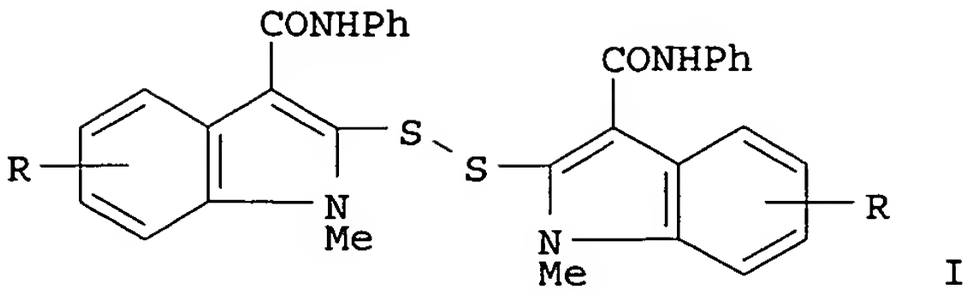
RN 158719-27-8 HCAPLUS
CN 1H-Indole-3-carboxamide, 2,2'-dithiobis[6-hydroxy-1-methyl-N-phenyl- (9CI) (CA INDEX NAME)



RN 158719-43-8 HCAPLUS
CN 1H-Indole-3-carboxamide, 2,2'-dithiobis[5-hydroxy-1-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L24 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:655576 HCAPLUS
DOCUMENT NUMBER: 121:255576
TITLE: Tyrosine Kinase Inhibitors. 3. Structure-Activity Relationships for Inhibition of Protein Tyrosine Kinases by Nuclear-Substituted Derivatives of 2,2'-Dithiobis(1-methyl-N-phenyl-1H-indole-3-carboxamide)
AUTHOR(S): Rewcastle, Gordon W.; Palmer, Brian D.; Dobrusin, Ellen M.; Fry, David W.; Kraker, Alan J.; Denny, William A.
CORPORATE SOURCE: School of Medicine, University of Auckland, Auckland, N. Z.
SOURCE: Journal of Medicinal Chemistry (1994), 37(13), 2033-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Nov 1994
GI



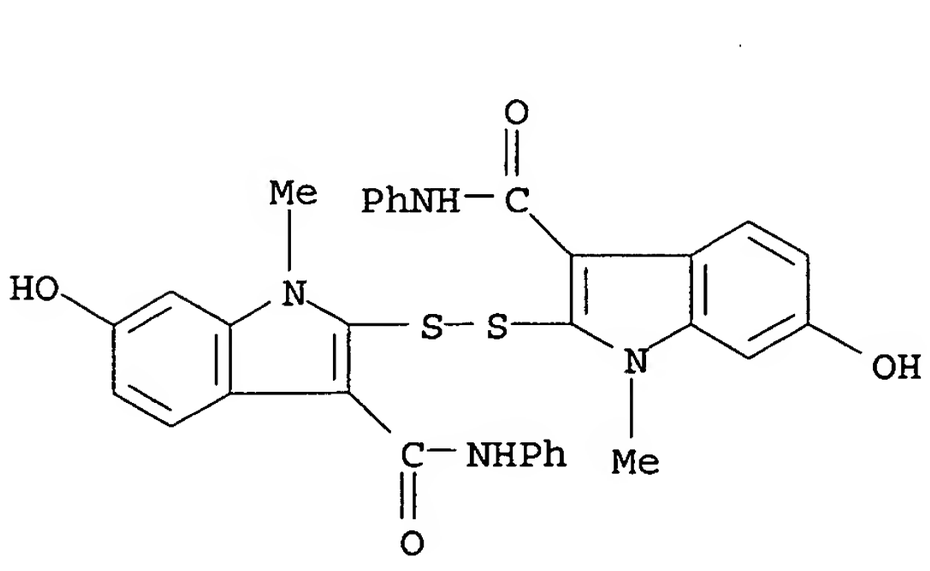
I

AB A series of indole-substituted 2,2'-dithiobis(1-methyl-N-phenyl-1H-indole-3-carboxamides) I (R = H, 5-Cl, 6-Me, 7-OH, 5-MeO, etc.) were prepared and evaluated for their ability to inhibit the tyrosine kinase activity of both the **epidermal** growth factor receptor (EGFR) and the nonreceptor pp60v-src tyrosine kinase. The compds. were synthesized by conversion of appropriate 1-methyloxindoles to 1-methyl-2-indolinethiones with P2S5 followed by subsequent reaction with NaH and Ph isocyanate and oxidative dimerization of the resulting 2,3-dihydro-N-phenyl-2-thioxo-1H-indole-3-carboxamides. The parent compound and many of the substituted analogs were moderately potent inhibitors of both kinase enzymes, but no clear relationships were seen between substitution on the indole ring and inhibitory activity. While 4-substituted compds. were generally inactive, 5-substituted derivs. with electron-withdrawing groups showed inhibitory activity. However, none of the substituted compds. showed significantly better activity than the unsubstituted parent compound There was generally a good correlation between activity against the EGFR and pp60v-src kinases, but several compds. did show some specificity (>20-fold) of inhibition; 5-Cl and 5-Br derivs. preferentially inhibited pp60v-src, while the 5-CF3 compound preferentially inhibited EGFR. Selected compds. from the series were found to inhibit the growth of Swiss 3T3 fibroblasts with IC50s in the range 2-25 μM, the most active being 4-substituted derivs. The compds. inhibited bFGF-mediated protein tyrosine phosphorylation in intact cells more effectively than EGFR- or PDGF-mediated phosphorylation.

IT **158719-27-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and protein tyrosine kinases inhibition by)

RN 158719-27-8 HCAPLUS

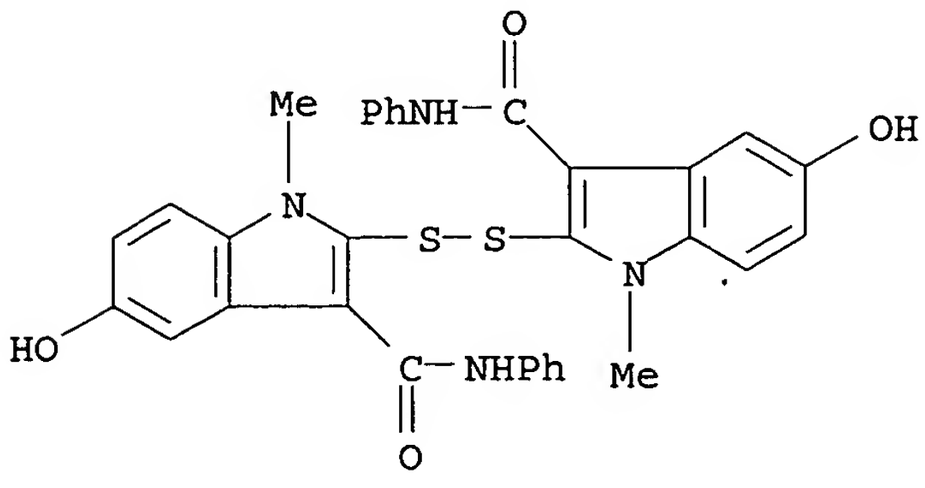
CN 1H-Indole-3-carboxamide, 2,2'-dithiobis[6-hydroxy-1-methyl-N-phenyl- (9CI) (CA INDEX NAME)



IT **158719-43-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 158719-43-8 HCAPLUS

CN 1H-Indole-3-carboxamide, 2,2'-dithiobis[5-hydroxy-1-methyl-N-phenyl- (9CI) (CA INDEX NAME)



L24 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:483050 HCAPLUS
DOCUMENT NUMBER: 121:83050
TITLE: Preparation of 2-indolinethiones and related disulfides and seleno-analogs as protein tyrosine kinase inhibitors and antitumor agents
INVENTOR(S): Dobrusin, Ellen Myra; Showalter, Howard Daniel Hollis; Denny, William Alexander; Palmer, Brian Desmond; Rewcastle, Gordon William; Tercel, Moana; Thompson, Andrew Mark
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 212 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9403427	A1	19940217	WO 1993-US7272		19930802
W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, RU, SK					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 654024	A1	19950524	EP 1993-918594		19930802
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
HU 71553	A2	19951228	HU 1995-341		19930802
JP 08503450	T2	19960416	JP 1993-519671		19930802
AU 672224	B2	19960926	AU 1993-47994		19930802
AU 9347994	A1	19940303			
CZ 283965	B6	19980715	CZ 1995-288		19930802
NZ 255194	A	20000128	NZ 1993-255194		19930802
RU 2155187	C2	20000827	RU 1995-108332		19930802
SK 283413	B6	20030701	SK 1995-135		19930802
PRIORITY APPLN. INFO.:			US 1992-926015	A	19920806
			WO 1993-US7272	W	19930802

OTHER SOURCE(S): MARPAT 121:83050
ED Entered STN: 20 Aug 1994
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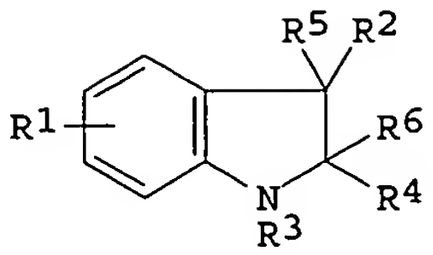

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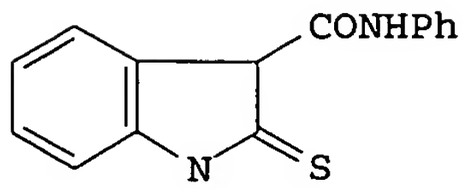
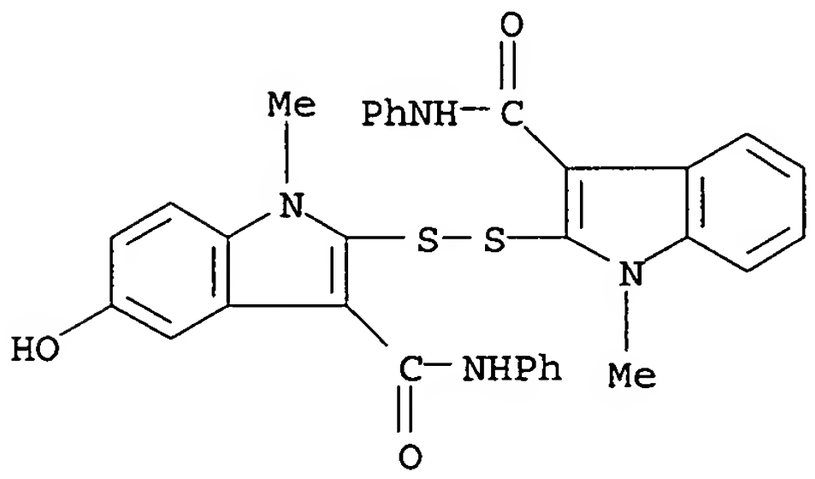


II

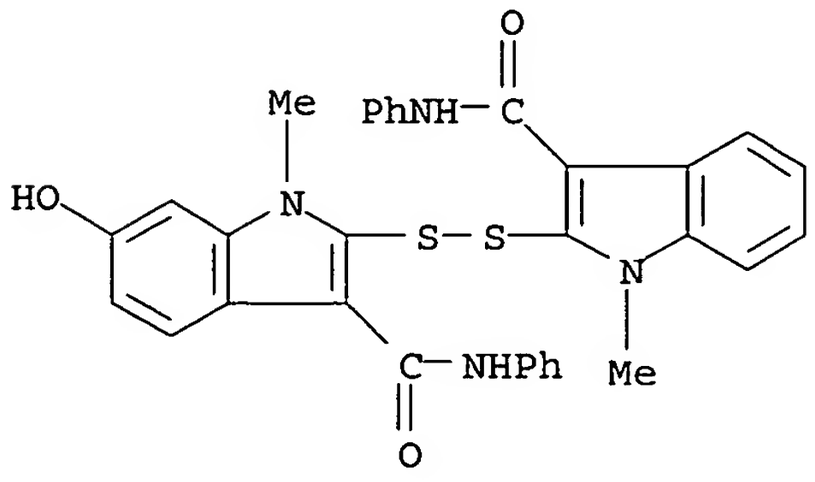
AB Title compds. [I; R1 = H, halo, OH, alkyl, alkoxy, CO2H, etc.; 1 or 2 CR1 = N; R2 = (acyl)alkyl, CH:CHCO2H, alkylcarbabamoyl, acyl, etc.; R3 = H, alkyl, CH2Ph; R4 = ZH, ZnX, ZnQ; R5 = H and R4R6 = S or Se; R5R6 = bond; Q = I in which R4 = Zn and R5R6 = bond; X = H, alkyl, CH2Ph, (hetero)aryl; Z = S, Se; n = 0-3] were prepared Thus, 1-methyl-2-indolinone was treated with P2S5 and the product treated with NaH and PhNCO to give indolinethionecarboxamide II which had IC50 of 2μM against **epidermal** growth factor mediated mitogenisis.

IT **156136-06-0P 156136-08-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as protein tyrosine kinase inhibitor)

RN 156136-06-0 HCAPLUS
CN 1H-Indole-3-carboxamide, 5-hydroxy-1-methyl-2-[[1-methyl-3-[(phenylamino)carbonyl]-1H-indol-2-yl]dithio]-N-phenyl- (9CI) (CA INDEX NAME)



RN 156136-08-2 HCAPLUS
CN 1H-Indole-3-carboxamide, 6-hydroxy-1-methyl-2-[[1-methyl-3-[(phenylamino)carbonyl]-1H-indol-2-yl]dithio]-N-phenyl- (9CI) (CA INDEX NAME)



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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  New CAS Information Use Policies, enter HELP USAGETERMS for details.

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  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.


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L26       10594 SEA FILE=CAOLD ABB=ON  PLU=ON  SKIN OR ?DERM?
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L25  ANSWER 1 OF 2  CAOLD  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:  CA56:10075b  CAOLD
TITLE:             quinones - (XXXVII) condensation of p-benzoquinone with
                   anilides of β-aminocrotonic acids
AUTHOR NAME:       Grinev, A. N.; Ermakova, V. N.; Mel'nikova, I. A.;
                   Terent'ev, A. P.
INDEX TERM:         636-41-9    930-87-0    936-12-9   1003-29-8   1072-83-9
                   2199-49-7   2703-17-5  18519-26-1  91556-85-3  92966-88-6
                   93331-34-1  93648-69-2  94298-69-8  95021-07-1
                   95426-91-8  95433-09-3 100324-49-0
IT  93331-34-1
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CN   Indole-3-carboxanilide, 5-hydroxy-1,2-dimethyl- (7CI)  (CA INDEX NAME)
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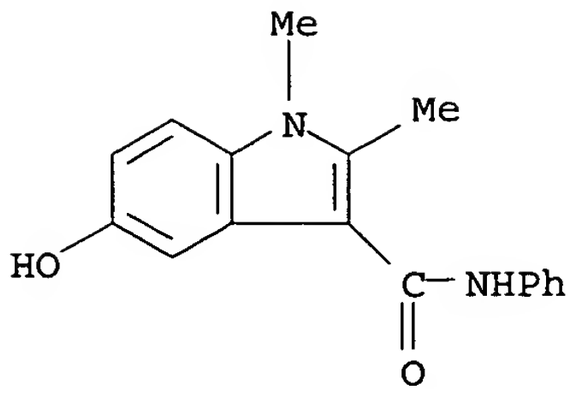
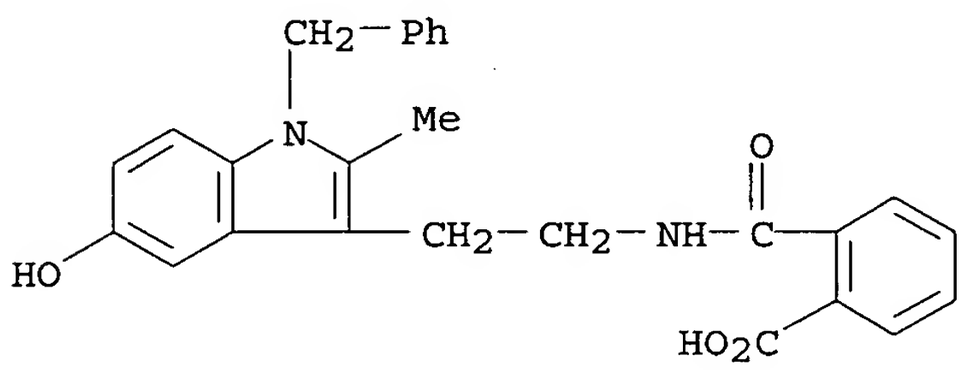


L25 ANSWER 2 OF 2 CAOLD COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: CA54:16652h CAOLD
TITLE: highly potent antimetabolites of serotonin with little serotoninlike action
AUTHOR NAME: Woolley, Dilworth W.
INDEX TERM: 2016-57-1 102240-53-9 102458-33-3 **102948-03-8** 102951-82-6 103211-57-0 103389-62-4 104339-40-4 104397-63-9 104399-16-8 106166-19-2 109018-10-2 122702-01-6
IT **102948-03-8**
RN 102948-03-8 CAOLD
CN Phthalamic acid, N-[2-(1-benzyl-5-hydroxy-2-methylindol-3-yl)ethyl]- (6CI) (CA INDEX NAME)



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               SEL RN

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               E KIETZMANN M?/AU
               E KIETZMANN M/AU
               E HOPPMANN J/AU
               E BAUMER W/AU
               E BAEUMER W/AU
               E KUSS H/AU
               E HOFGEN N/AU
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               HOPPMANN J?/AU OR BAUMER W?/AU OR BAEUMER W?/AU OR KUSS H?/AU
               OR HOFGEN N?/AU
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L20        2341 SEA ABB=ON  PLU=ON  INTEGUMENT?
L21           4 SEA ABB=ON  PLU=ON  L13 AND (L18 OR L19 OR L20)
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L22      384518 SEA ABB=ON  PLU=ON  SKIN OR ?DERM?
L23          17 SEA ABB=ON  PLU=ON  L13 AND L22
L24          17 SEA ABB=ON  PLU=ON  L23 OR L21
                D SCAN TI

      FILE 'CAOLD' ENTERED AT 15:07:51 ON 22 SEP 2006
L25           2 SEA ABB=ON  PLU=ON  L12
                D SCAN
L26       10594 SEA ABB=ON  PLU=ON  SKIN OR ?DERM?
L27           0 SEA ABB=ON  PLU=ON  L25 AND L26

      FILE 'REGISTRY' ENTERED AT 15:09:42 ON 22 SEP 2006
                D STAT QUE L12

      FILE 'HCAPLUS' ENTERED AT 15:09:59 ON 22 SEP 2006
                D QUE NOS L24
                D IBIB ED ABS HITSTR L24 1-17

      FILE 'CAOLD' ENTERED AT 15:10:52 ON 22 SEP 2006
                D STAT QUE NOS L25
                D STAT QUE NOS L26
                D STAT QUE NOS L27
                D IALL HITSTR L25 1-2

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FILE CAPLUS

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FILE HCAPLUS

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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